

Connecting via Winsock to STN

Welcome to STN International! Enter x:x

LOGINID:sssptal633cxq

PASSWORD:

TERMINAL (ENTER 1, 2, 3, OR ?):2

\* \* \* \* \* Welcome to STN International \* \* \* \* \*  
\* \*

NEWS	1		Web Page for STN Seminar Schedule - N. America
NEWS	2	APR 04	STN AnaVist, Version 1, to be discontinued
NEWS	3	APR 15	WPIDS, WPINDEX, and WPIX enhanced with new predefined hit display formats
NEWS	4	APR 28	EMBASE Controlled Term thesaurus enhanced
NEWS	5	APR 28	IMSRESEARCH reloaded with enhancements
NEWS	6	MAY 30	INPAFAMDB now available on STN for patent family searching
NEWS	7	MAY 30	DGENE, PCTGEN, and USGENE enhanced with new homology sequence search option
NEWS	8	JUN 06	EPFULL enhanced with 260,000 English abstracts
NEWS	9	JUN 06	KOREAPAT updated with 41,000 documents
NEWS	10	JUN 13	USPATFULL and USPAT2 updated with 11-character patent numbers for U.S. applications
NEWS	11	JUN 19	CAS REGISTRY includes selected substances from web-based collections
NEWS	12	JUN 25	CA/CAPplus and USPAT databases updated with IPC reclassification data
NEWS	13	JUN 30	AEROSPACE enhanced with more than 1 million U.S. patent records
NEWS	14	JUN 30	EMBASE, EMBAL, and LEMBASE updated with additional options to display authors and affiliated organizations
NEWS	15	JUN 30	STN on the Web enhanced with new STN AnaVist Assistant and BLAST plug-in
NEWS	16	JUN 30	STN AnaVist enhanced with database content from EPFULL
NEWS	17	JUL 28	CA/CAPplus patent coverage enhanced
NEWS	18	JUL 28	EPFULL enhanced with additional legal status information from the epoline Register
NEWS	19	JUL 28	IFICDB, IFIPAT, and IFIUDB reloaded with enhancements
NEWS	20	JUL 28	STN Viewer performance improved
NEWS	21	AUG 01	INPADOCDB and INPAFAMDB coverage enhanced
NEWS	22	AUG 13	CA/CAPplus enhanced with printed Chemical Abstracts

page images from 1967-1998

NEWS 23 AUG 15 CAOLD to be discontinued on December 31, 2008

NEWS 24 AUG 15 Caplus currency for Korean patents enhanced

NEWS 25 AUG 25 CA/Caplus, CASREACT, and IFI and USPAT databases enhanced for more flexible patent number searching

NEWS 26 AUG 27 CAS definition of basic patents expanded to ensure comprehensive access to substance and sequence information

NEWS EXPRESS JUNE 27 08 CURRENT WINDOWS VERSION IS V8.3,  
AND CURRENT DISCOVER FILE IS DATED 23 JUNE 2008.

NEWS HOURS STN Operating Hours Plus Help Desk Availability

NEWS LOGIN Welcome Banner and News Items

NEWS IPC8 For general information regarding STN implementation of IPC 8

Enter NEWS followed by the item number or name to see news on that specific topic.

All use of STN is subject to the provisions of the STN Customer agreement. Please note that this agreement limits use to scientific research. Use for software development or design or implementation of commercial gateways or other similar uses is prohibited and may result in loss of user privileges and other penalties.

\* \* \* \* \* STN Columbus \* \* \* \* \*

FILE 'HOME' ENTERED AT 15:24:37 ON 02 SEP 2008

=> FIL BIOSIS CAPLUS EMBASE  
COST IN U.S. DOLLARS

	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	0.63	0.63

FILE 'BIOSIS' ENTERED AT 15:26:25 ON 02 SEP 2008  
Copyright (c) 2008 The Thomson Corporation

FILE 'CAPLUS' ENTERED AT 15:26:25 ON 02 SEP 2008  
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.  
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.  
COPYRIGHT (C) 2008 AMERICAN CHEMICAL SOCIETY (ACS)

FILE 'EMBASE' ENTERED AT 15:26:25 ON 02 SEP 2008  
Copyright (c) 2008 Elsevier B.V. All rights reserved.

=> s mRNA (3a) instabil? sequence  
L1 19 MRNA (3A) INSTABIL? SEQUENCE

=> s mRNA (3a) instabil?  
L2 964 MRNA (3A) INSTABIL?

=> s l1 and APP

L3 0 L1 AND APP

=> s l2 and APP

L4 3 L2 AND APP

=> dup rem l4

PROCESSING COMPLETED FOR L4

L5 3 DUP REM L4 (0 DUPLICATES REMOVED)

=> d bib abs 1-

YOU HAVE REQUESTED DATA FROM 3 ANSWERS - CONTINUE? Y/(N):y

L5 ANSWER 1 OF 3 CAPLUS COPYRIGHT 2008 ACS on STN

AN 2004:999715 CAPLUS

DN 141:406751

TI Assay and expression systems comprising reporter gene and  
instability

sequence DNA for identifying compounds which affect stability of  
mRNA

IN Kastelic, Tania; Cheneval, Dominique

PA Novation Pharmaceuticals Inc., Can.

SO U.S. Pat. Appl. Publ., 49 pp., Cont.-in-part of U.S. Ser. No.  
869,159.

CODEN: USXXCO

DT Patent

LA English

FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.
--	------------	------	------	-----------------

DATE				
------	--	--	--	--

PI	US 20040231007	A1	20041118	US 2004-814634
----	----------------	----	----------	----------------

	20040401			
--	----------	--	--	--

	WO 2000039314	A1	20000706	WO 1999-CA1235
--	---------------	----	----------	----------------

	19991223			
--	----------	--	--	--

W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN,

CR, CU,

CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU,

ID, IL,

IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU,

LV, MA,

MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE,

SG, SI,

SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA,

ZW

RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH,

CY, DE,

DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF,

BJ, CF,

CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

AU 2005229165	A1	20051013	AU 2005-229165
20050401			
CA 2603585	A1	20051013	CA 2005-2603585
20050401			
WO 2005095615	A1	20051013	WO 2005-CA491
20050401			

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW

RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

EP 1774000	A1	20070418	EP 2005-730094
20050401			

R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR

JP 2007530058	T	20071101	JP 2007-505349
20050401			

US 20070190532	A1	20070816	US 2007-594851
20070504			

PRAI GB 1998-28709	A	19981224
WO 1999-CA1235	W	19991223
US 2001-869159	A2	20010815
US 2004-814634	A	20040401
WO 2005-CA491	W	20050401

AB The present invention relates to an assay for the identification of biol.

active compds., in particular to a reporter gene assay for the identification of compds., which have an effect on mRNA stability. More

particularly, the present invention relates to a reporter gene expression

system and cell lines comprising said expression system. The invention

further relates to compds. which destabilize mRNA. Radicicol and radicicol analog A showed a clear effect on mRNA stability.

Human

APP, Bcl-2 $\alpha$ , c-myc, TNF $\alpha$ , IL-1 $\beta$ , VEGF instability sequence were constructed. Instability sequence DNA is from The gene encoding a cytokine, a gene encoding a chemokine, a gene encoding a nuclear transcription factor, a gene encoding an oxygenase, a proto-oncogene, an immediate early gene, a cell cycle controlling gene, and a gene involved in apoptosis.

L5 ANSWER 2 OF 3 CAPLUS COPYRIGHT 2008 ACS on STN

AN 2000:5273 CAPLUS

DN 132:147542

TI Growth factor-mediated stabilization of amyloid precursor protein mRNA is mediated by a conserved 29-nucleotide sequence in the 3'-untranslated region

AU Rajagopalan, Lakshman E.; Malter, James S.

CS Department of Pathology and Laboratory Medicine, University of Wisconsin

Medical School, Madison, WI, 53792, USA

SO Journal of Neurochemistry (2000), 74(1), 52-59

CODEN: JONRA9; ISSN: 0022-3042

PB Lippincott Williams & Wilkins

DT Journal

LA English

AB Using a cell-free translation system, we previously demonstrated that the turnover and translation of amyloid precursor protein (APP) mRNA was regulated by a 29-nucleotide instability element, located 200 nucleotides downstream from the stop codon. Here we have examined the

regulatory role of this element in primary human capillary endothelial

cells under different nutritional conditions. Optimal proliferation

required a growth medium (endothelial cell growth medium) supplemented

with epidermal, basic fibroblast, insulin-like, and vascular endothelial

growth factors. In vitro transcribed mRNAs with the

5'-untranslated

region (UTR) and coding region of  $\beta$ -globin and the entire 3'-UTR of

APP 751 were transfected into cells cultured in endothelial cell growth medium. Wild-type globin-APP mRNA containing an intact APP 3'-UTR and mutant globin-APP mRNA containing a mutated 29-nucleotide element decayed with identical half-lives ( $t_{1/2}$  = 60 min).

Removal of all supplemental growth factors from the culture medium

significantly accelerated the decay of transfected wild-type mRNA ( $t_{1/2}$  = 10 min), but caused only a moderate decrease in the half-life of transfected mutant mRNA ( $t_{1/2}$  = 40 min). We therefore conclude that the 29-nucleotide 3'-UTR element is an mRNA destabilizer whose function can be inhibited by inclusion of the aforementioned mixture of growth factors in the culture medium.

RE.CNT 47      THERE ARE 47 CITED REFERENCES AVAILABLE FOR THIS RECORD  
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5      ANSWER 3 OF 3    CAPLUS    COPYRIGHT 2008 ACS on STN

AN      1996:187915    CAPLUS

DN      124:252087

OREF 124:46496h,46497a

TI      Interactions of INS (CRS) elements and the splicing machinery regulate the

production of Rev-responsive mRNAs

AU      Mikaelian, Ivan; Krieg, Marion; Gait, Michael J.; Karn, Jonathan

CS      MRC Lab. Mol. Biol., Cambridge, CB2 2QH, UK

SO      Journal of Molecular Biology (1996), 257(2), 246-64

CODEN: JMOBAK; ISSN: 0022-2836

PB      Academic

DT      Journal

LA      English

AB      The human immunodeficiency virus type 1 (HIV-1) Rev protein stimulates the

export to the cytoplasm of unspliced HIV-1 mRNAs carrying the Rev response

element (RRE). However, simple addition of the RRE to  $\beta$ -globin pre-mRNA

does not confer a Rev response on this heterologous transcript. In this

paper, the authors demonstrate that a strong Rev response is conferred on

$\beta$ -globin pre-mRNA when an inhibitory (INS) elements is inserted into

the gene together with the RRE. In the presence of the INS element, Rev

was able to stimulate the export to the cytoplasm of unspliced mRNA 10 to

15-fold. INS elements from the HIV-1 p17 gag and pol genes were equally

active in complementing Rev-dependent nuclear export of unspliced mRNA.

By contrast, mutated p17 gag INS element, known to be inactive in gag

mRNA instability assays, was unable to complement the

Rev/RRE system and stimulate nuclear export. Similarly,

AUUUA-instability

elements from the granulocyte-macrophage colony stimulating factor mRNA (GM-CSF) destabilized  $\beta$ -globin mRNA but could not substitute for the HIV INS elements. Complementation between the Rev/RRE system and the INS elements was only observed when splicing was efficient. When splicing of the  $\beta$ -globin gene receptor is impaired by mutations in the 5' splicing of the  $\beta$ -globin gene receptor is impaired by mutations in the 5' splice donor, the 3' splice acceptor sequence, or the polypyrimidine tract, the majority of the unspliced mRNA is exported from the nucleus in the absence of Rev. In the presence of splice site mutations, Rev is able to act independently of a functional INS element and increase the export of unspliced mRNA three to fivefold. The authors propose that nuclear factor(s) binding to INS elements sep. unspliced  $\beta$ -globin pre-mRNA from the splicing apparatus Pre-mRNA in this "INS compartment" remains accessible to Rev. Thus, there is a synergy between the INS elements and accessible to Rev. Thus, there is a synergy between the INS elements and Rev which leads to enhanced nuclear export of unspliced mRNA.

=> FIL STNGUIDE

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	40.74	41.37
DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	-2.40	
-2.40		

FILE 'STNGUIDE' ENTERED AT 15:38:21 ON 02 SEP 2008  
 USE IS SUBJECT TO THE TERMS OF YOUR CUSTOMER AGREEMENT  
 COPYRIGHT (C) 2008 AMERICAN CHEMICAL SOCIETY (ACS)

FILE CONTAINS CURRENT INFORMATION.  
 LAST RELOADED: Aug 29, 2008 (20080829/UP).

=> FIL BIOSIS CAPLUS EMBASE

COST IN U.S. DOLLARS	SINCE FILE	TOTAL
----------------------	------------	-------

	ENTRY	SESSION
FULL ESTIMATED COST	0.30	41.67
DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE	TOTAL
CA SUBSCRIBER PRICE	ENTRY	SESSION
-2.40	0.00	

FILE 'BIOSIS' ENTERED AT 15:41:06 ON 02 SEP 2008  
 Copyright (c) 2008 The Thomson Corporation

FILE 'CAPLUS' ENTERED AT 15:41:06 ON 02 SEP 2008  
 USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.  
 PLEASE SEE "HELP USAGETERMS" FOR DETAILS.  
 COPYRIGHT (C) 2008 AMERICAN CHEMICAL SOCIETY (ACS)

FILE 'EMBASE' ENTERED AT 15:41:06 ON 02 SEP 2008  
 Copyright (c) 2008 Elsevier B.V. All rights reserved.

=> s l2 and bcl-2  
 L6 10 L2 AND BCL-2

=> dup rem l6  
 PROCESSING COMPLETED FOR L6  
 L7 6 DUP REM L6 (4 DUPLICATES REMOVED)

=> d bib abs 1-  
 YOU HAVE REQUESTED DATA FROM 6 ANSWERS - CONTINUE? Y/(N):y

L7 ANSWER 1 OF 6 BIOSIS COPYRIGHT (c) 2008 The Thomson  
 Corporation on STN

DUPLICATE 1

AN 2008:342473 BIOSIS

DN PREV200800342472

TI The nucleolin targeting aptamer AS1411 destabilizes bcl-  
 2 messenger RNA in human breast cancer cells.

AU Soundararajan, Sridharan; Chen, Weiwei; Spicer, Eleanor K.;  
 Courtenay-Luck, Nigel; Fernandes, Daniel J. [Reprint Author]

CS Med Univ S Carolina, Dept Biochem and Mol Biol, 176 Ashley Ave,  
 Charleston, SC 29425 USA  
 fernand@musc.edu

SO Cancer Research, (APR 1 2008) Vol. 68, No. 7, pp. 2358-2365.  
 CODEN: CNREA8. ISSN: 0008-5472.

DT Article

LA English

ED Entered STN: 11 Jun 2008

Last Updated on STN: 11 Jun 2008

AB sought to determine whether nucleolin, a bcl-2  
 mRNA-binding protein, has a role in the regulation of bcl-  
 2 mRNA stability in MCF-7 and MDA-MB-231 breast cancer cells.  
 Furthermore, we examined the efficacy of the aptamer AS1411 in  
 targeting



nucleolin and inducing bcl-2 mRNA  
instability and cytotoxicity in these cells. AS1411 at 5 mu  
mol/L  
inhibited the growth of MCF-7 and MDA-MB-231 cells, whereas 20  
mu mol/L  
AS1411 had no effect on the growth rate or viability of normal  
MCF-10A  
mammary epithelial cells. This selectivity of AS1411 was  
related to a  
greater uptake of AS1411 into the cytoplasm of MCF-7 cells  
compared with  
MCF-10A cells and to a 4-fold higher level of cytoplasmic  
nucleolin in  
MCF-7 cells. Stable siRNA knockdown of nucleolin in MCF-7 cells  
reduced  
nucleolin and bcl-2 protein levels and decreased the  
half-life of bcl-2 mRNA from 11 to 5 hours.  
Similarly, AS1411 (10 mu mol/L) decreased the half-life of bcl-  
2 mRNA in MCF-7 and MDA-MB-231 cells to 1.0 and 1.2 hours,  
respectively. In contrast, AS1411 had no effect on the  
stability of  
bcl-2 mRNA in normal MCF-10A cells. AS1411 also  
inhibited the binding of nucleolin to the instability element  
AU-rich  
element 1 of bcl-2 mRNA in a cell-free system and in  
MCF-7 cells. Together, the results suggest that AS1411 acts as a  
molecular decoy by competing with bcl-2 mRNA for  
binding to cytoplasmic nucleolin in these breast cancer cell  
lines. This  
interferes with the stabilization of bcl-2 mRNA by  
nucleolin and may be one mechanism by which AS1411 induces tumor  
cell  
death.

L7 ANSWER 2 OF 6 BIOSIS COPYRIGHT (c) 2008 The Thomson  
Corporation on STN

AN 2006:182353 BIOSIS

DN PREV200600184465

TI Mode of action of rituximab in chronic lymphocytic leukaemia;  
Activation

of Tis11b, an inducer of mRNA instability, and  
induction of apoptosis.

AU Baou, Maria [Reprint Author]; Murphy, John; Jewell, Andrew P.

CS Kingston Univ, Sch Life Sci, Surrey, UK

SO Blood, (NOV 16 2005) Vol. 106, No. 11, Part 1, pp. 593A.

Meeting Info.: 47th Annual Meeting of the  
American-Society-of-Hematology.

Atlanta, GA, USA. December 10 -13, 2005. Amer Soc Hematol.

CODEN: BLOOAW. ISSN: 0006-4971.

DT Conference; (Meeting)

LA English

ED Entered STN: 15 Mar 2006

Last Updated on STN: 5 Jun 2008

AB Rituximab is a chimeric anti-CD20 monoclonal antibody that has been used successfully in the treatment of Non Hodgkin's Lymphoma or patients with Chronic Lymphocytic Leukaemia (CLL). The mechanisms of action of Rituximab are not fully understood although antibody dependent cell mediated cytotoxicity and complement dependent cytotoxicity have been shown to be important. An alternative mechanism is the induction of apoptosis through activation of pathways mediated through CD20. CD20 is involved in many cellular processes including proliferation, activation, differentiation and apoptosis. We have found that treatment of CILL cells with 20  $\mu$ g/ml Rituximab cross-linked will) a secondary antibody reduced cell viability from 84  $\pm$  8% (in unstimulated cells) to 51.50  $\pm$  10% after 48h of cultivation by the Annexin/PI method. Using inhibitors specific for p38, JNK and ERK pathways, we found that inhibition of p38 inhibits the induction of apoptosis by crosslinked Rituximab. Rituximab has been reported to inhibit this pathway and lead to down regulation of bcl-2 expression in AIDS related lymphoma cells. However the mechanism is unclear. One mechanism by which many genes involved in apoptosis are regulated is through induction of mRNA instability through induction of Tis 11 family genes. The Tis I family (Tis 11, Tis 11b/Berg36 and Tis 11d) bind to AU Rich elements present in several mRNA (eg bcl-2, TNF) and cause their degradation. We found that Tis 11b/Berg36 is strongly induced by crosslinked Rituximab. Tis I Id was weakly induced while Tis I I remained unchanged after treatment. Furthermore we found that induction of Tis 11b/Berg36 by Rituximab is partly regulated through the p38 pathway since inhibition of this pathway resulted partial or complete inhibition of Tis 11b/Berg36 induction. This suggests that Tis 11b/Berg36 may mediate the induction of apoptosis by Rituximab through the degradation of proteins

involved in apoptosis that contain AU Rich elements, disrupting  
autoocrine  
cytokine feedback mechanisms and down regulating bcl-2

L7 ANSWER 3 OF 6 BIOSIS COPYRIGHT (c) 2008 The Thomson  
Corporation on STN

DUPLICATE 2

AN 2005:126151 BIOSIS

DN PREV200500121589

TI Retinoid-induced apoptosis in HL-60 cells is associated with  
nucleolin

down-regulation and destabilization of bcl-2 mRNA.

AU Otake, Yoko; Sengupta, Tapas K.; Bandyopadhyay, Sumita; Spicer,  
Eleanor

K.; Fernandes, Daniel J. [Reprint Author]

CS Dept Biochem and Mol Biol, Med Univ S Carolina, 173 Ashley  
Ave, POB 250509,

Charleston, SC, 29425, USA

fernand@musc.edu

SO Molecular Pharmacology, (January 2005) Vol. 67, No. 1, pp.  
319-326. print.

ISSN: 0026-895X (ISSN print).

DT Article

LA English

ED Entered STN: 1 Apr 2005

Last Updated on STN: 1 Apr 2005

AB All-trans retinoic acid ( ATRA) induces differentiation of  
promyelocytic

leukemia cells, but the mechanisms by which cellular  
differentiation leads

to apoptosis are not well understood. Studies were done to  
address the

question whether ATRA-induced apoptosis is a consequence of  
destabilization of bcl-2 mRNA and decreased cellular  
levels of the anti-apoptotic protein, bcl-2. ATRA

induced differentiation of HL-60 cells along the granulocytic  
pathway

within 48 h. The half-lives of bcl-2 mRNA in HL-60

cells incubated with ATRA for 48 or 72 h were reduced to 39 and  
7% of the

corresponding untreated control values, respectively. Cellular  
differentiation was accompanied by down-regulation of the

cytoplasmic

levels of nucleolin, a bcl-2 mRNA-stabilizing protein.

Binding of a bcl-2 mRNA instability

element (AU- rich element-1) to nucleolin in S100 extracts from  
ATRA-treated cells was decreased to 15% of control within 72 h.

The decay

of 5' capped, polyadenylated bcl-2 mRNA transcripts

containing ARE-1 was more rapid in S100 extracts from

ATRA-treated cells

compared with untreated cells. However, when recombinant nucleolin was added to extracts of ATRA-treated cells, the rate of bcl-2 mRNA decay was similar to the rate in extracts of untreated cells. These results provide evidence that ATRA-induced apoptosis is a consequence of cellular differentiation, which leads to nucleolin down-regulation and bcl-2 mRNA instability.

L7 ANSWER 4 OF 6 CAPLUS COPYRIGHT 2008 ACS on STN

AN 2004:999715 CAPLUS

DN 141:406751

TI Assay and expression systems comprising reporter gene and instability

sequence DNA for identifying compounds which affect stability of mRNA

IN Kastelic, Tania; Cheneval, Dominique

PA Novation Pharmaceuticals Inc., Can.

SO U.S. Pat. Appl. Publ., 49 pp., Cont.-in-part of U.S. Ser. No. 869,159.

CODEN: USXXCO

DT Patent

LA English

FAN.CNT 2

DATE	PATENT NO.	KIND	DATE	APPLICATION NO.
PI	US 20040231007	A1	20041118	US 2004-814634
20040401				
	WO 2000039314	A1	20000706	WO 1999-CA1235
19991223				
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	AU 2005229165	A1	20051013	AU 2005-229165
20050401				
	CA 2603585	A1	20051013	CA 2005-2603585
20050401				

WO 2005095615                      A1              20051013              WO 2005-CA491  
20050401  
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ,  
CA, CH,  
CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI,  
GB, GD,  
GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR,  
KZ, LC,  
LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ,  
NA, NI,  
NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK,  
SL, SM,  
SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU,  
ZA, ZM, ZW  
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM,  
ZW, AM,  
AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ,  
DE, DK,  
EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL,  
PL, PT,  
RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ,  
GW, ML,  
MR, NE, SN, TD, TG

EP 1774000                      A1              20070418              EP 2005-730094  
20050401  
R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR,  
HU, IE,  
IS, IT, LI, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR  
JP 2007530058                      T              20071101              JP 2007-505349  
20050401  
US 20070190532                      A1              20070816              US 2007-594851  
20070504

PRAI GB 1998-28709                      A              19981224  
WO 1999-CA1235                      W              19991223  
US 2001-869159                      A2              20010815  
US 2004-814634                      A              20040401  
WO 2005-CA491                      W              20050401

AB The present invention relates to an assay for the identification of biol.

active compds., in particular to a reporter gene assay for the identification of compds., which have an effect on mRNA stability. More

particularly, the present invention relates to a reporter gene expression

system and cell lines comprising said expression system. The invention

further relates to compds. which destabilize mRNA. Radicicol and radicicol analog A showed a clear effect on mRNA stability.

Human APP,

Bcl-2.alpha., c-myc, TNF $\alpha$ , IL-1 $\beta$ , VEGF

instability sequence were constructed. Instability sequence DNA is from

The gene encoding a cytokine, a gene encoding a chemokine, a gene encoding a nuclear transcription factor, a gene encoding an oxygenase, a proto-oncogene, an immediate early gene, a cell cycle controlling gene, and a gene involved in apoptosis.

L7 ANSWER 5 OF 6 CAPLUS COPYRIGHT 2008 ACS on STN

AN 2005:208720 CAPLUS

DN 143:41672

TI Mitochondrial DNA microsatellite instability and expression of Bcl

-2 and Bax mRNA in gastric cancer and its precancerous lesions

AU Fang, Dianchun; Ling, Xianlong; Luo, Yuanhui

CS Research and Treatment Center for Digestive Diseases of PLA, Southwest

Hospital, Third Military Medical University, Chongqing, 400038, Peop. Rep. China

SO Jiefangjun Yixue Zazhi (2003), 28(11), 982-984

CODEN: CFCHBN; ISSN: 0577-7402

PB Jenminjun Chubanshe

DT Journal

LA Chinese

AB The relation between mitochondrial DNA microsatellite instability (mtMSI)

and the expression of Bcl-2 and Bax mRNA in gastric cancer and precancerous lesions was studied. MtMSI and

expression of

Bcl-2 and Bax mRNA were detected with PCR-SSCP and RT-PCR, resp. Expression of Bcl-2 mRNA in intestinal metaplasia (IM, 53.3%) and dysplasia (Dys, 70%) were

significantly higher

than that in normal control tissue (10%), whereas no significant differences were found among chronic gastritis (CAG, 50%),

gastric cancer

(GC, 30%) and normal controls. Expression of Bcl-2

mRNA in Dys was higher than that in GC. Expression of Bax mRNA

was

significantly increased in Dys (60%), but not in CAG (50%), IM (46.7%) and

GC (33.3), compared with normal control (10%). Expression of Bcl-2 and Bax mRNA in Helicobacter pylori infected gastric mucosa was significantly higher than that in non-H. pylori infected

gastric

mucosa, but expression of Bcl-2 and Bax mRNA were not

consistent with H. pylori CagA status. MtMSI levels were 0,

10.0, 13.3,

20.0, and 36.7% in controls, CAG, IM, Dys, and GC, resp. No

significant

difference was found between the expression of Bcl-2

and Bax mRNA in mtMSI(+) and that in mtMSI(-) tissues. MtMSI

may play an

important role in some gastric cancers, and increased mtMSI is independent of abnormal expression of Bcl-2 and Bax mRNA.

L7 ANSWER 6 OF 6 CAPLUS COPYRIGHT 2008 ACS on STN  
 AN 2002:240751 CAPLUS  
 DN 136:279323  
 TI Preparation of lactone-containing benzoate esters and their use as

pharmaceutical use

IN Kastelic, Tania; Cheneval, Dominique; Leutwiler, Albert

PA Novation Pharmaceuticals Inc., Can.

SO PCT Int. Appl., 57 pp.

CODEN: PIXXD2

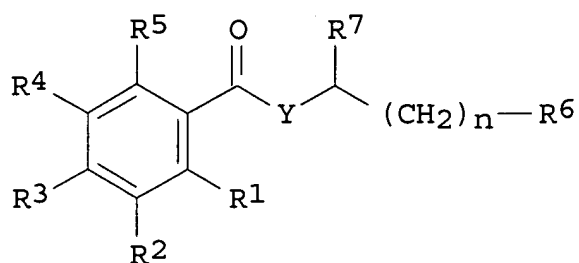
DT Patent

LA English

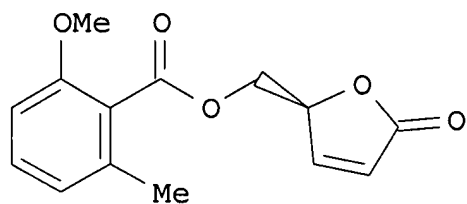
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.
WO 2002024674	A1	20020328	WO 2001-CA1331
20010921			
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW			
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			
CA 2420185	A1	20020328	CA 2001-2420185
20010921			
AU 2001093555	A	20020402	AU 2001-93555
20010921			
EP 1318991	A1	20030618	EP 2001-973891
20010921			
EP 1318991	B1	20060816	
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR			
JP 2004509167	T	20040325	JP 2002-529084
20010921			

AT 336487	T	20060915	AT 2001-973891
20010921			
ES 2276829	T3	20070701	ES 2001-973891
20010921			
US 20050049202	A1	20050303	US 2003-381294
20030321			
PRAI CA 2000-2320664	A	20000921	
WO 2001-CA1331	W	20010921	
OS MARPAT 136:279323			
GI			



I



II

AB The title compds. [I; R1-R5 = H, OH, halogen, (C1-4) alkyl, (C1-4) alkenyl, (C1-4) alkoxy, (C1-4) alkyl-CO2; Y = O, NR; R = H, (C1-4) alkyl; n = 0-8; R6 = 5-8-membered (un)substituted (un)saturated lactone or lactam ring; R7 = H, (C1-4) alkyl, (C1-4) alkenyl, (C1-4) alkoxy, Ph, (C1-4) alkyl-CO2], which are useful for the treatment or prevention of disorders with an etiol. associated with or comprising excessive cytokine release and are also used in the treatment of cancer, inflammatory disorders and disorders associated with an increased stability of mRNA which has an mRNA instability sequence; I-containing pharmaceutical formulation are presented. Compound II, prepared via esterification of the corresponding chiral hydroxymethyl-substituted lactone with



2-methoxy-6-methylbenzoic acid, demonstrated activity against  
THP-1 cell  
lines.

RE.CNT 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD  
ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> s bcl2 and AU  
L8 43 BCL2 AND AU

=> dup rem l8  
PROCESSING COMPLETED FOR L8  
L9 36 DUP REM L8 (7 DUPLICATES REMOVED)

=> s l9 and PY<=1998  
L10 5 L9 AND PY<=1998

=> d bib abs 1-  
YOU HAVE REQUESTED DATA FROM 5 ANSWERS - CONTINUE? Y/(N):y

L10 ANSWER 1 OF 5 BIOSIS COPYRIGHT (c) 2008 The Thomson  
Corporation on STN  
AN 1997:199800 BIOSIS  
DN PREV199799499003  
TI Peripheral blood stem cell CD34+ autologous transplant in  
relapsed  
follicular lymphoma.  
AU Marin, G. H.; Dal Cortivo, L.; Cayuela, J. M.; Marolleau, J. P.;  
Pautier,  
P.; Cojean-Zelek, I.; Brice, P.; Makke, J.; Benbunan, M.;  
Gisselbrecht, C.  
[Reprint author]  
CS Serv. Reanimation Hematol. Adulte, Hopital Saint-Louis, 1 avenue  
Claude  
Vellefaux, F-75475 Paris cedex 10, France  
SO Hematology and Cell Therapy, (1997) Vol. 39, No. 1, pp. 33-40.  
ISSN: 1269-3286.  
DT Article  
LA English  
ED Entered STN: 12 May 1997  
Last Updated on STN: 12 May 1997  
AB To evaluate CD34+ selection of peripheral blood stem cells  
(PBSC) as a  
graft for autologous transplantation. Eight relapsing  
follicular lymphoma  
(FL) patients were submitted to CD34+ autologous stem cell  
transplantation  
(ASCT). All patients received at least two front line  
conventional  
therapies; mean time to treatment failure (TTF) was 4.5 months.  
Patients  
had disseminated stage III-IV disease after a median number of  
2.1

relapses. Chemotherapy and G-CSF were used as mobilization for leukapheresis. CEPRATE SC concentrator (Cell Pro, Inc, Bothell, WA) was used to select CD34+ cells from leukapheresis products. With a mean of 1.8 leukaphereses per patient,  $8.1 \times 10^{-8}$  mononuclear cells (MNCs)/kg were collected. After the selection process, the median number of MNCs was  $9.4 \times 10^{-6}$ /kg;  $4.3 \times 10^{-6}$ /kg CD34+ cells and  $17 \times 10^{-4}$ /kg CFU-GM, with a purity of 83.7% and a viability of 89.2%. Mbr bcl2 /IgH PCR analysis of 5 grafts showed that initial buffy-coat, and CD34- fractions were negative in 3 cases and positive in 2 cases (from whom selected CD34+ fraction remained positive in 1 case). After a conditioning regimen including total body irradiation, cyclophosphamide and etoposide, CD34+ selected cells were reinfused. AU patients but one had successful engraftment, median time to WBC  $gt 1 \times 10^{-9}/l$  was 12 days and platelets  $gt 50 \times 10^{-9}/l$  17 days. No severe infectious complications were seen. After transplant, with a minimum follow up of 2 years, 5 patients are still in complete remission (CR). Three patients have relapsed after 1 year of transplant with a mean TTF of 15.6 months. We conclude that PBSC CD34+ selection for ASCT was a safe technique, capable of reconstituting hemopoiesis without severe complications for high risk FL patients included in this study. The effects of tumor cell purging need to be evaluated in a larger series.

L10 ANSWER 2 OF 5 BIOSIS COPYRIGHT (c) 2008 The Thomson Corporation on STN

AN 1994:485444 BIOSIS

DN PREV199497498444

TI Differential induction of apoptosis in human breast tumor cells by okadaic

acid and related inhibitors of protein phosphatases 1 and 2A.

AU Kiguchi, Kaoru; Glesne, David; Chubb, Cynthia H.; Fujiki, Hirota; Huberman, Eliezer [Reprint author]

CS Argonne National Lab., 9700 S. Cass Ave., Argonne, IL 60439, USA  
SO Cell Growth and Differentiation, (1994) Vol. 5, No. 9, pp. 995-1004.

ISSN: 1044-9523.

DT Article

LA English

ED Entered STN: 9 Nov 1994

Last Updated on STN: 16 Dec 1994

AB To investigate a possible relationship between apoptosis induction and

protein phosphorylation in human breast carcinoma cells, we treated three

such cell types, MB231, MCF-7, and AU-565, with okadaic acid (OA), an inhibitor of protein phosphatases 1 and 2A, or phorbol

12

myristate 1 3-acetate, an activator of protein kinase C. We

then examined

these cells for the appearance of apoptosis markers. While OA caused

multiplication arrest and cytotoxicity in all three cell lines, apoptosis

was induced in MB-231 and MCF-7 cells but not in AU565 cells. A similar

cell-specific apoptosis induction was also observed after treatment with

dinophysistoxin-1 (an active OA analogue) and with calyculin A (a structurally unrelated protein phosphatase inhibitor) but not

with

analogues that either are inactive or penetrate epithelial cells poorly.

Phorbol 12-myristate 13-acetate also inhibited cell multiplication but was

without effect in inducing apoptosis in these cells. Levels of the

apoptosis-inhibitory protein BCL2 were examined in these cells, but they did not correlate with this differential

susceptibility. We

additionally treated the three cell types with 1-beta-D-arabinofuranosylcytosine and genistein to determine whether the

AU

-565 cell line would also be resistant to apoptosis induction by other

chemical stimuli. Both of these agents led to the induction of apoptosis

in all three cell lines. These results indicate that the AU-565 cells are specifically resistant to apoptosis induction by

inhibitors of

protein phosphatases 1 and 2A. This cell-specific resistance may thus

allow one to identify cellular mediators of apoptosis by comparing protein

phosphorylation patterns in these cells before and after treatment with OA

or related inhibitors.

L10 ANSWER 3 OF 5 CAPLUS COPYRIGHT 2008 ACS on STN

AN 1996:463418 CAPLUS

DN 125:139307

OREF 125:26029a,26032a

TI A bcl-2/IgH antisense transcript deregulates bcl-2 gene expression in

human follicular lymphoma t(14;18) cell lines

AU Capaccioli, S.; Quattrone, A.; Schiavone, N.; Calastretti, A.; Copreni,

E.; Bevilacqua, A.; Canti, G.; Gong, L.; Morelli, S.; Nicolin, A.

CS Inst. Gen. Pathol., Univ. Florence, Florence, 50134, Italy

SO Oncogene (1996), 13(1), 105-115

CODEN: ONCNES; ISSN: 0950-9232

PB Stockton

DT Journal

LA English

AB The 14;18 chromosome translocation, characteristic of most human follicular B-cell lymphomas, juxtaposes the bcl-2 gene with the IgH locus,

creating a bcl-2/IgH hybrid gene. By mechanisms that are still under

investigation, this event increases the cellular levels of the bcl-2 mRNA

and thereby induces an overprod. of the antiapoptotic BCL-2 protein which

is likely responsible for neoplastic transformation. In an effort to

identify potential upregulators of bcl-2 activity in t(14;18) cells, a

bcl-2 antisense transcript was found by strand-specific RT-PCR that is

present in the t(14;18) DOHH2 and SU-DHL-4 but not in the t(14;18)-neg.

Raji and Jurkat lymphoid cell lines, and thus appears to be dependent on

the bcl-2/IgH fusion. This antisense transcript is a hybrid bcl-2/IgH

RNA, that originates in the IgH locus, encompasses the t(14;18) fusion

site and spans at least the complete 3' UTR region of the bcl-2 mRNA. To

achieve some insight into its biol. function, the t(14;18) DOHH2 cell line

was treated with oligonucleotides (ODNs) by specifically targeting the

bcl-2/IgH antisense strand. These ODNs lowered bcl-2 gene expression and

inhibited neoplastic cell growth by inducing apoptosis. Thus, the

bcl-2/IgH antisense transcript may contribute, by an unknown mechanism, to

upregulation of bcl-2 gene expression in t(14;18) cells. The possibility

has been considered that the hybrid antisense transcript mask AU

-rich motifs present in the 3' UTR of the bcl-2 mRNA characterized in other genes as mRNA destabilizing elements.

L10 ANSWER 4 OF 5 CAPLUS COPYRIGHT 2008 ACS on STN

AN 1996:183430 CAPLUS

DN 124:285072

OREF 124:52719a,52722a

TI BCL-2 expression or antioxidants prevent hyperglycemia-induced formation

of intracellular advanced glycation endproducts in bovine endothelial cells

AU Giardino, Ida; Edelstein, Diane; Brownlee, Michael

CS Department of Medicine, Albert Einstein College of Medicine, New York, NY, 10461, USA

SO Journal of Clinical Investigation (1996), 97(6), 1422-8  
CODEN: JCINAO; ISSN: 0021-9738

PB Rockefeller University Press

DT Journal

LA English

AB Hyperglycemia rapidly induces an increase in intracellular advanced

glycation end products (AGEs) in bovine endothelial cells, causing an alteration in bFGF activity. Because sugar or sugar-adduct autoxidn. is

critical for AGE formation in vitro, the role of reactive oxygen species

(ROS) in intracellular AGE formation was evaluated by using bovine aortic

endothelial cells. Glucose (30 mM) increased intracellular ROS formation

by 250% and lipid peroxidn. by 330%, while not affecting ROS in the media.

In cells depleted of glutathione, intracellular AGE accumulation increased

linearly with ROS generation as measured by immunoblotting and the

fluorescent probe DCFH (AGE 0.258-3.531 AU\* mm/5 + 104 cells, DCF 57-149 mean AU, r = 0.998, P < 0.002). Deferoxamine,  $\alpha$ -tocopherol, and dimethylsulfoxide each inhibited hyperglycemia-induced formation of both ROS and AGE. To

differentiate an

effect of ROS generation on AGE formation from an effect of more distal

oxidative processes, GM7373 endothelial cell lines were generated that

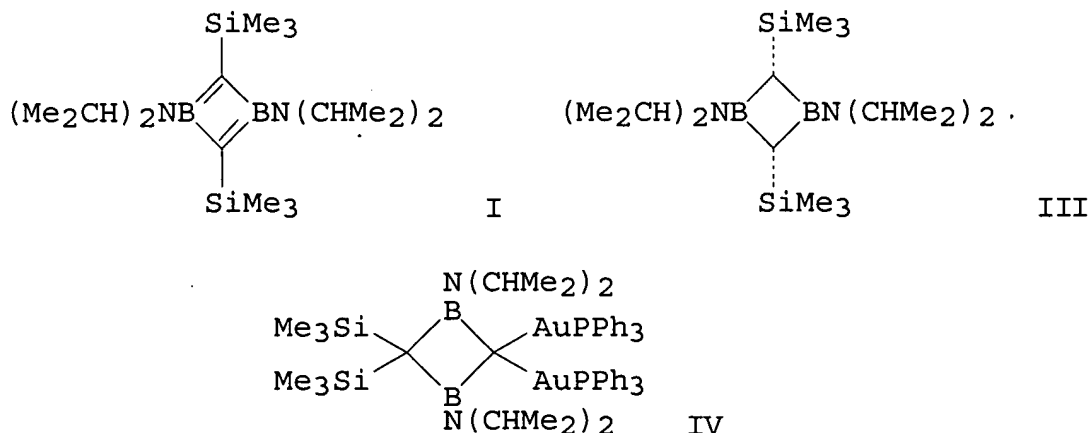
stably expressed the peroxidn.-suppressing proto-oncogene bcl-2.

Bcl-2

had no effect on hyperglycemia-induced intracellular ROS formation. In

contrast, bcl-2 expression decreased both lipid peroxidn. (100% at 3 h and 29% at 168 h) and AGE formation (55% at 168 h). These data show that a ROS-dependent process plays a central role in the generation of intracellular AGEs, and that inhibition of oxidant pathways prevents intracellular AGE formation.

L10 ANSWER 5 OF 5 CAPLUS COPYRIGHT 2008 ACS on STN  
 AN 1987:33148 CAPLUS  
 DN 106:33148  
 OREF 106:5567a,5570a  
 TI A folded and a planar 1,3-diboretane  
 AU Hornbach, Pia; Hildenbrand, Manfred; Pritzkow, Hans; Siebert, Walter  
 CS Anorg.-Chem. Inst., Univ. Heidelberg, Heidelberg, D-6900, Fed. Rep. Ger.  
 SO Angewandte Chemie (1986), 98(12), 1121-3  
 CODEN: ANCEAD; ISSN: 0044-8249  
 DT Journal  
 LA German  
 OS CASREACT 106:33148  
 GI



AB Treatment of B<sub>2</sub>Cl<sub>4</sub> with Me<sub>3</sub>SiC.tplbond.CSiMe<sub>3</sub> gave (Me<sub>3</sub>Si)<sub>2</sub>C:C(BCl<sub>2</sub>)<sub>2</sub> which was treated with (Me<sub>2</sub>CH)<sub>2</sub>NH to give (Me<sub>3</sub>Si)<sub>2</sub>C:C[BClN(CHMe<sub>2</sub>)<sub>2</sub>]<sub>2</sub>. Treatment of the latter compound with NaK<sub>8</sub> gave the diborate I which gave a stable dianion (II) by treatment with more NaK<sub>8</sub>. Hydrogenation of I gave the diboretane III which was also obtained by treating II with CHCl<sub>3</sub> or HN(SiMe<sub>3</sub>)<sub>2</sub>. Treatment of II with Ph<sub>3</sub>PAuCl

gave the Au derivative IV.

=> FIL STNGUIDE

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	54.54	96.21
DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE -7.20	-4.80	

FILE 'STNGUIDE' ENTERED AT 15:49:29 ON 02 SEP 2008  
USE IS SUBJECT TO THE TERMS OF YOUR CUSTOMER AGREEMENT  
COPYRIGHT (C) 2008 AMERICAN CHEMICAL SOCIETY (ACS)

FILE CONTAINS CURRENT INFORMATION.  
LAST RELOADED: Aug 29, 2008 (20080829/UP).

=> FIL BIOSIS CAPLUS EMBASE

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	0.06	96.27
DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE -7.20	0.00	

FILE 'BIOSIS' ENTERED AT 15:49:55 ON 02 SEP 2008  
Copyright (c) 2008 The Thomson Corporation

FILE 'CAPLUS' ENTERED AT 15:49:55 ON 02 SEP 2008  
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.  
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.  
COPYRIGHT (C) 2008 AMERICAN CHEMICAL SOCIETY (ACS)

FILE 'EMBASE' ENTERED AT 15:49:55 ON 02 SEP 2008  
Copyright (c) 2008 Elsevier B.V. All rights reserved.

=> d his

(FILE 'HOME' ENTERED AT 15:24:37 ON 02 SEP 2008)

FILE 'BIOSIS, CAPLUS, EMBASE' ENTERED AT 15:26:25 ON 02 SEP 2008

L1	19 S MRNA (3A) INSTABIL? SEQUENCE
L2	964 S MRNA (3A) INSTABIL?
L3	0 S L1 AND APP
L4	3 S L2 AND APP
L5	3 DUP REM L4 (0 DUPLICATES REMOVED)

FILE 'STNGUIDE' ENTERED AT 15:38:21 ON 02 SEP 2008

FILE 'BIOSIS, CAPLUS, EMBASE' ENTERED AT 15:41:06 ON 02 SEP 2008

L6 10 S L2 AND BCL-2  
L7 6 DUP REM L6 (4 DUPLICATES REMOVED)  
L8 43 S BCL2 AND AU  
L9 36 DUP REM L8 (7 DUPLICATES REMOVED)  
L10 5 S L9 AND PY<=1998

FILE 'STNGUIDE' ENTERED AT 15:49:29 ON 02 SEP 2008

FILE 'BIOSIS, CAPLUS, EMBASE' ENTERED AT 15:49:55 ON 02 SEP 2008

=> s BCL 2 and (ARE or AU)

L11 28853 BCL 2 AND (ARE OR AU)

=> FIL STNGUIDE

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	11.53	107.80

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	0.00	
-7.20		

FILE 'STNGUIDE' ENTERED AT 15:52:15 ON 02 SEP 2008

USE IS SUBJECT TO THE TERMS OF YOUR CUSTOMER AGREEMENT  
COPYRIGHT (C) 2008 AMERICAN CHEMICAL SOCIETY (ACS)

FILE CONTAINS CURRENT INFORMATION.

LAST RELOADED: Aug 29, 2008 (20080829/UP).

=> FIL BIOSIS CAPLUS EMBASE

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	0.36	108.16

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	0.00	
-7.20		

FILE 'BIOSIS' ENTERED AT 15:56:07 ON 02 SEP 2008

Copyright (c) 2008 The Thomson Corporation

FILE 'CAPLUS' ENTERED AT 15:56:07 ON 02 SEP 2008

USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.

PLEASE SEE "HELP USAGETERMS" FOR DETAILS.

COPYRIGHT (C) 2008 AMERICAN CHEMICAL SOCIETY (ACS)

FILE 'EMBASE' ENTERED AT 15:56:07 ON 02 SEP 2008



Copyright (c) 2008 Elsevier B.V. All rights reserved.

=> s AU (3a) rich  
L12 3839 AU (3A) RICH

=> s l12 and BCL 2  
L13 57 L12 AND BCL 2

=> s l13 and py<=1998  
L14 3 L13 AND PY<=1998

=> dup rem l14  
PROCESSING COMPLETED FOR L14  
L15 1 DUP REM L14 (2 DUPLICATES REMOVED)

=> d bib abs

L15 ANSWER 1 OF 1 BIOSIS COPYRIGHT (c) 2008 The Thomson  
Corporation on STN

DUPLICATE 1

AN 1996:414837 BIOSIS

DN PREV199699137193

TI A bcl-2/IgH antisense transcript deregulates  
bcl-2 gene expression in human follicular lymphoma  
t(14;18) cell lines.

AU Capaccioli, S.; Quattrone, A.; Schiavone, N.; Calastretti, A.;  
Copreni,

E.; Bevilacqua, A.; Canti, G.; Gong, L.; Morelli, S.; Nicolin,  
A. [Reprint  
author]

CS Dep. Pharmacol., Sch. Med., Via Vanvitelli 32, 20129 Milan, Italy

SO Oncogene, (1996) Vol. 13, No. 1, pp. 105-115.

CODEN: ONCNES. ISSN: 0950-9232.

DT Article

LA English

ED Entered STN: 10 Sep 1996

Last Updated on STN: 10 Sep 1996

AB The 14;18 chromosome translocation, characteristic of most human  
follicular B-cell lymphomas, juxtaposes the bcl-2 gene  
with the IgH locus, creating a bcl-2/IgH hybrid gene.

By mechanisms that are still under investigation, this event  
increases the

cellular levels of the bcl-2 mRNA and thereby induces  
an overproduction of the antiapoptotic BCL-2 protein  
which is likely responsible for neoplastic transformation. In  
an effort

to identify potential upregulators of bcl-2 activity  
in t(14;18) cells, we found, by strand-specific RT-PCR, a hcl-2  
antisense

transcript that is present in the t(14;18) DOHH2 and SU-DHL-4  
but not in

the t(14;18)-negative Raji and Jurkat lymphoid cell lines, and  
thus

appears to be dependent on the bcl-2/IgH fusion. This antisense transcript is a hybrid bcl-2/IgH RNA, that originates in the IgH locus, encompasses the t(14;18) fusion site and spans at least the complete 3' UTR region of the bcl-2 mRNA. To achieve some insight into its biological function, we treated the t(14;18) DOHH2 cell line with oligonucleotides (ODNs) by specifically targeting the bcl-2/IgH antisense strand. These ODNs lowered bcl-2 gene expression, inhibited neoplastic cell growth by inducing apoptosis. We would like to propose the hypothesis that the bcl-2/IgH antisense transcript may contribute, by an unknown mechanism, to upregulation of bcl-2 gene expression in t(14;18) cells. The possibility has been considered that the hybrid antisense transcript mask AU-rich motifs present in the 3' UTR of the bcl-2 mRNA characterized in other genes as mRNA destabilizing elements.

=> FIL STNGUIDE

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	16.95	125.11
DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	0.00	
-7.20		

FILE 'STNGUIDE' ENTERED AT 15:58:18 ON 02 SEP 2008  
 USE IS SUBJECT TO THE TERMS OF YOUR CUSTOMER AGREEMENT  
 COPYRIGHT (C) 2008 AMERICAN CHEMICAL SOCIETY (ACS)

FILE CONTAINS CURRENT INFORMATION.  
 LAST RELOADED: Aug 29, 2008 (20080829/UP).

=> FIL BIOSIS CAPLUS EMBASE

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	0.06	125.17
DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	0.00	
-7.20		

FILE 'BIOSIS' ENTERED AT 15:58:39 ON 02 SEP 2008  
 Copyright (c) 2008 The Thomson Corporation

FILE 'CAPLUS' ENTERED AT 15:58:39 ON 02 SEP 2008  
 USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.

PLEASE SEE "HELP USAGETERMS" FOR DETAILS.  
COPYRIGHT (C) 2008 AMERICAN CHEMICAL SOCIETY (ACS)

FILE 'EMBASE' ENTERED AT 15:58:39 ON 02 SEP 2008  
Copyright (c) 2008 Elsevier B.V. All rights reserved.

=> s mRNA (3a) stabil?  
L16 18718 MRNA (3A) STABIL?

=> s l16 and bcl 2  
L17 120 L16 AND BCL 2

=> s l17 and pY<=1998  
L18 10 L17 AND PY<=1998

=> dup rem l18  
PROCESSING COMPLETED FOR L18  
L19 5 DUP REM L18 (5 DUPLICATES REMOVED)

=> d bib abs 1-  
YOU HAVE REQUESTED DATA FROM 5 ANSWERS - CONTINUE? Y/(N):y

L19 ANSWER 1 OF 5 CAPLUS COPYRIGHT 2008 ACS on STN  
AN 1998:672675 CAPLUS  
DN 129:271496  
OREF 129:55245a,55248a  
TI Viral vectors for identification of RNA regulatory sequences and  
interacting molecules  
IN Blau, Helen M.; Spicher, Albert; Guicherit, Oivin  
PA The Board of Trustees of the Leland Stanford Junior University,  
USA  
SO PCT Int. Appl., 64 pp.  
CODEN: PIXXD2  
DT Patent  
LA English  
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.
--	------------	------	------	-----------------

DATE	-----	----	-----	-----
------	-------	------	-------	-------

PI	WO 9842854	A1	19981001	WO 1998-US6093
----	------------	----	----------	----------------

19980327 <--  
W: CA, JP  
RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC,  
NL, PT, SE

PRAI US 1997-42543P P 19970327

AB Methods and compns. for the identification, characterization and  
isolation

of regulatory RNA sequences are provided. Regulatory RNA  
sequences

mediate post-transcriptional regulation in response to various  
environmental conditions and can be used to alter the level of  
expression

of endogenous genes or to identify factors which interact with regulatory RNA sequences. The invention addnl. provides improved vector systems for rapid screening, anal., and tightly-regulated expression of regulatory RNA sequences. The regulatory properties of highly conserved regions (HCRs) within 3'-UTRs that have retained greater than 70% homol. within stretches of 100 nucleotides over 30 million years were examined. A retroviral vector system was used with a selectable marker that allowed rapid delivery of 3'-UTR-reporter constructs to populations of thousands of cells within one to two weeks, avoiding problems associated with clonal anal. and long-term selection. Addnl., this vector is modular, thereby permitting direct comparison of different HCRs on gene expression, independent of 5'-UTRs, promoters, protein coding regions and polyadenylation signals. Ten HCRs (from c-fos, c-myc, transferrin receptor, bcl2, EF1 $\alpha$ , vimentin, ornithine decarboxylase, fibronectin, HuD and Ran genes) were examined. Nine of these HCRs (i.e., all except the Ran HCR) were found to decrease mRNA stability to different extents. Two HCRs (the c-fos and vimentin HCRs) altered mRNA translation under steady-state conditions. Four HCRs (the HuD, Ran, fibronectin and ornithine decarboxylase HCRs) mediated responses to changes in mitogen level by increasing reporter protein levels 2-fold while 2 HCRs exhibited a 6-fold difference in their response to another environmental stress, hypoxia.

RE.CNT 8        THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD  
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L19 ANSWER 2 OF 5 BIOSIS COPYRIGHT (c) 2008 The Thomson Corporation on STN

DUPLICATE 1

AN 1997:160160 BIOSIS

DN PREV199799459363

TI Increased gadd153 messenger RNA level is associated with apoptosis in

human leukemic cells treated with etoposide.

AU Eymin, Beatrice; Dubrez, Laurence; Allouche, Michele; Solary, Eric

[Reprint author]

CS Lab. Oncohematol. Pharmacol., CJF INSERM 94-08, UFR  
Med./Pharmacy, 7

boulevard Jeanne d'Arc, 21033 Dijon, France

SO Cancer Research, (1997) Vol. 57, No. 4, pp. 686-695.  
CODEN: CNREA8. ISSN: 0008-5472.

DT Article

LA English

ED Entered STN: 15 Apr 1997

Last Updated on STN: 15 Apr 1997

AB Treatment of leukemic cells with topoisomerase inhibitors can  
lead to

growth arrest and subsequent apoptotic cell death. The  
relationships

between cell cycle regulation and apoptosis triggering remain  
poorly

understood. The gadd153 gene encodes the nuclear protein CHOP  
10 that

acts as a negative modulator of CCAAT/enhancer binding protein  
transcriptional factors and inhibits cell cycle progression. We  
have

investigated the relationships between gadd153 gene expression  
and

apoptosis induction in four human leukemic cell lines with  
different

sensitivities to apoptosis induced by etoposide (VP-16), a  
topoisomerase

11 inhibitor. The gadd153 gene was constitutively expressed in  
the four

studied cell lines. In U937 and HL-60 cells that were very  
sensitive to

apoptosis induction by the drug, VP-16 induced a time- and  
dosedependent

increase of gadd153 gene mRNA expression. Using agarose gel  
electrophoresis and a quantitative filter elution assay,

apoptotic DNA

fragmentation was observed to begin when gadd153 gene expression  
increased. Equitoxic doses of VP-16 (as defined using a 96-h  
3-4,5-dimethylthiazol-2,5-diphenyltetrazolium bromide assay) did  
not

increase the gadd153 mRNA level in K562 and KCL22 cell lines  
that were

more resistant to apoptosis induction by the drug. Nuclear  
run-on and

mRNA stability experiments demonstrated that VP-16

treatment increased gadd153 gene transcription in the sensitive  
U937

cells. Cycloheximide did not prevent gadd153 expression  
increase. Both

gadd153 mRNA level increase and internucleosomal DNA  
fragmentation were

inhibited by N-tosyl-L-phenylalanine chloromethylketone, a serine

threonine protease inhibitor,  
N-acetyl-leucyl-leucyl-norleucinal, an  
inhibitor of calpain, N-acetylcysteine, an inhibitor of oxidative  
metabolism, and overexpression of Bcl-2. Z-VAD and  
Z-DEVD peptides that inhibit interleukin 1-beta-converting  
enzyme-like  
proteases suppressed DNA fragmentation without preventing  
gadd153 mRNA  
increase in VP-16-treated U937 cells. These results indicate  
that gadd153  
gene expression increase occurs downstream of events sensitive to  
N-tosyl-L-phenylalanine chloromethylketone, calpain inhibitor I,  
and  
Bcl-2 and upstream of interleukin 1-beta-converting  
enzyme-related proteases activation in leukemic cells in which  
treatment  
with VP-16 induces rapid apoptosis.

L19 ANSWER 3 OF 5 EMBASE COPYRIGHT (c) 2008 Elsevier B.V. All  
rights

reserved on STN  
AN 1997289087 EMBASE  
TI Dexamethasone suppresses apoptosis in a human gastric cancer  
cell line  
through modulation of bcl-x gene expression.  
AU Chang, Tsu-Chung (correspondence); Chu, Jing-Tsai; Chu, Li-Ling  
CS Department of Biochemistry, Natl. Def. Med. Ctr., P.O. B.,  
Taipei, Taiwan,  
Province of China.  
AU Hung, Mei-Whey; Tsai, Lai-Chen  
CS Department of Medical Research, Veterans General Hospital,  
Taipei, Taiwan,  
Province of China.  
AU Jiang, Shu-Yang  
CS Grad. Institute of Medical Sciences, National Defense Medical  
Center,  
Taipei, Taiwan, Province of China.  
AU Chang, Tsu-Chung (correspondence)  
CS Department of Biochemistry, National Defence Medical Center, PO  
Box  
90048-501, Taipei, Taiwan, Province of China.  
SO FEBS Letters, (22 Sep 1997) Vol. 415, No. 1, pp. 11-15.  
Refs: 26  
ISSN: 0014-5793 CODEN: FEBLAL  
PUI S 0014-5793(97)01083-1  
CY Netherlands  
DT Journal; Article  
FS 016 Cancer  
029 Clinical and Experimental Biochemistry  
037 Drug Literature Index  
LA English  
SL English

ED Entered STN: 9 Oct 1997  
Last Updated on STN: 9 Oct 1997  
AB Treatment of human gastric cancer TMK-1 cells with transcription and translation inhibitors rapidly triggered cell apoptosis. Along with cell apoptosis, the Bcl-x(S) level was markedly upregulated suggesting a crucial role of this protein in promoting tile apoptotic process. In the presence of dexamethasone, however, cell apoptosis was greatly attenuated as demonstrated by DNA histogram shift and DNA fragmentation. Studies using the glucocorticoid receptor antagonist RU486 indicated that attenuation of apoptosis was mediated through glucocorticoid receptors. Dexamethasone not only suppressed the apoptosis-associated upregulation of Bcl-x(S) but also enhanced the basal level of Bcl-x(L) in the cells. In addition, bcl-x mRNA stability was significantly extended in the presence of dexamethasone, These results indicate that dexamethasone exerted a protective effect and delayed apoptosis of TMK-1 cells by modulating bcl-x gene expression.

L19 ANSWER 4 OF 5 BIOSIS COPYRIGHT (c) 2008 The Thomson Corporation on STN

DUPLICATE 2

AN 1997:42737 BIOSIS

DN PREV199799334725

TI Modulation of apoptosis-associated genes bcl-2, bcl-x, and bax during rat liver regeneration.

AU Kren, Betsy T.; Trembley, Janeen H.; Krajewski, Stanislaw; Behrens,

Timothy W.; Reed, John C.; Steer, Clifford J. [Reprint author]

CS Dep. Med., Univ. Minnesota Med. Sch., Box 36 UMHC, 516 Delaware Street SE,

Minneapolis, MN 55455, USA

SO Cell Growth and Differentiation, (1996) Vol. 7, No. 12, pp. 1633-1642.

ISSN: 1044-9523.

DT Article

LA English

ED Entered STN: 28 Jan 1997

Last Updated on STN: 28 Jan 1997

AB Liver regeneration (LR) after 70% partial hepatectomy (pH) represents a

unique in vivo model of cell cycle and gene regulation. This study was

conducted to characterize apoptosis-associated gene expression during LR.

The results indicated that transcripts for both bcl-x and bcl-2 exhibited similar patterns of expression during LR with peaks at

6 h post-PH. In contrast, the major 1.1-kb bax transcript exhibited peaks

at 18 (P lt 0.05) and 72 h (P lt 0.001) post-PH. Nuclear run-on analyses

for all three genes indicated no detectable transcription rate changes

during LR. At 6 h post-PH, when bcl-x mRNA levels were increased by

25-fold (P lt 0.001), bcl-x mRNA half-life was elevated 4-fold (P lt

0.001). Similarly, bax transcript half-life increased from 2.8 h at 0 h

to 4.3 h at 24 h (P lt 0.001) and gt 8 h at 40 h (P lt 0.001) post-PH,

coincident with increases in steady-state levels of mRNA.

Western blot

analyses of Bcl-2 and Bcl-x proteins showed no

significant change through 96 h of LR, whereas Bax protein

levels cycled

in parallel with its mRNA. Interestingly, novel Bax- and Bcl-2-cross-reactive proteins of 31 and 32 kDa, respectively, were detected in nuclei isolated from quiescent liver. When liver

growth was

induced by the peroxisome proliferator clofibrate, transcript and protein

levels were coupled for bcl-x but not for bax. In conclusion, the

apoptosis-associated genes bcl-2, bcl-x and bax are

modulated at the transcript and protein levels during LR,

suggesting a

role for these gene products in normal liver growth. The

alterations in

transcript levels occur posttranscriptionally and involve changes in

mRNA stability. Furthermore, unlike bax, steady-state

protein and transcript levels are uncoupled for both bcl-

2 and bcl-x, suggesting a role for translational regulation

during

LR after PH.

L19 ANSWER 5 OF 5 CAPLUS COPYRIGHT 2008 ACS on STN DUPLICATE 3

AN 1989:592378 CAPLUS

DN 111:192378

OREF 111:31935a,31938a

TI Regulation of bcl-2 gene expression in lymphoid cell lines containing normal #18 or t(14;18) chromosomes

AU Reed, John C.; Tsujimoto, Yoshihide; Epstein, Scott F.; Cuddy, Michael;



Slabiak, Trina; Nowell, Peter C.; Croce, Carlo M.  
 CS Sch. Med., Univ. Pennsylvania, Philadelphia, PA, 19104-6082, USA  
 SO Oncogene Research (1989), 4(4), 271-82  
 CODEN: ONCGE7; ISSN: 0890-6467  
 DT Journal  
 LA English  
 AB The bcl-2 (B cell lymphoma/leukemia-2) gene at band  
 18q21 is involved in t(14;18) chromosomal translocations in most  
 follicular lymphomas and occasional other human B cell  
 malignancies, where  
 it becomes juxtaposed to the transcriptionally active Ig (Ig)  
 locus at  
 14q32. Regulation of bcl-2 gene expression was  
 investigated in neoplastic lymphoid cell lines containing normal  
 #18  
 chromosomes or a t(14;18) translocation with regard to  
 steady-state  
 mRNA levels, RNA stability, transcription rates, and DNA  
 methylation. High steady-state levels of bcl-2 mRNA,  
 and proportionally high rates of bcl-2 transcription  
 (measured in isolated nuclei), were found in B cell lines  
 containing t(14;18)  
 translocations. The half-life of bcl-2 mRNA was  
 similar in all cell lines examined, including a  
 t(14;18)-containing follicular  
 lymphoma cell line, which has a translocated and rearranged bcl-  
 2 gene that produces bcl-2/Ig fusion  
 transcripts. However, in the presence of cycloheximide  
 (inhibitor of  
 protein synthesis), the half-life of some of the bcl-2  
 /Ig mRNAs produced by these cells was prolonged, indicating that  
 in some  
 circumstances mRNA stability may contribute to  
 deregulated bcl-2 expression. Despite stabilizing  
 some bcl-2 mRNAs, the overall effect of treating cell  
 lines with cycloheximide was a reduction in the levels of  
 accumulated  
 bcl-2 mRNAs through inhibition of bcl-  
 2 gene transcription. These latter data provide indirect  
 evidence  
 that short-lived transacting factor(s) regulate transcription of  
 the human  
 bcl-2 gene in lymphoid cells with or without a t(14;18)  
 translocation. No clear correlation was discovered between bcl-  
 2 gene methylation and transcription.

=> s bcl 2 alpha  
 L20 154 BCL 2 ALPHA

=> s 120 and ARE  
 L21 56 L20 AND ARE

=> dup rem 121

PROCESSING COMPLETED FOR L21

L22 36 DUP REM L21 (20 DUPLICATES REMOVED)

=> d bib abs 1-

YOU HAVE REQUESTED DATA FROM 36 ANSWERS - CONTINUE? Y/(N):y

L22 ANSWER 1 OF 36 CAPLUS COPYRIGHT 2008 ACS on STN

AN 2007:1116179 CAPLUS

DN 147:462499

TI Activation of melanocortin 4 receptors reduces the inflammatory response

and prevents apoptosis induced by lipopolysaccharide and interferon- $\gamma$  in astrocytes

AU Caruso, Carla; Durand, Daniela; Schioth, Helgi B.; Rey, Rodolfo; Seilicovich, Adriana; Lasaga, Mercedes

CS Centro de Investigaciones en Reproduccion, School of Medicine, University

of Buenos Aires, Buenos Aires, 1121ABG, Argent.

SO Endocrinology (2007), 148(10), 4918-4926

CODEN: ENDOAO; ISSN: 0013-7227

PB Endocrine Society

DT Journal

LA English

AB  $\alpha$ -MSH exerts an immunomodulatory action in the brain and may play a

neuroprotective role acting through melanocortin 4 receptor (MC4Rs). In

the present study, we show that MC4Rs are constitutively expressed in astrocytes as determined by immunocytochem.,

RT-PCR, and Western

blot anal.  $\alpha$ -MSH (5  $\mu$ M) reduced the nitric oxide production and the

expression of inducible nitric oxide synthase (iNOS) induced by bacterial

lipopolysaccharide (LPS, 1  $\mu$ g/mL) plus interferon- $\gamma$  (IFN- $\gamma$ , 50 ng/mL) in cultured astrocytes after 24 h.  $\alpha$ -MSH also

attenuated

the stimulatory effect of LPS/IFN- $\gamma$  on prostaglandin E2 release and

cyclooxygenase-2 (COX-2) expression. Treatment with HS 024, a selective

MC4R antagonist, blocked the antiinflammatory effects of  $\alpha$ -MSH, suggesting a MC4R-mediated mechanism in the action of this melanocortin.

In astrocytes, LPS/IFN- $\gamma$  treatment reduced cell viability, increased

the number of terminal deoxynucleotidyl transferase-mediated dUTP nick-end

labeling-pos. cells and activated caspase-3.  $\alpha$ -MSH prevented these

apoptotic events, and this cytoprotective effect was abolished by HS 024.

LPS/IFN- $\gamma$  decreased Bcl-2, whereas it increased Bax protein expression in astrocytes, thus increasing the Bax/Bcl-2 ratio.  $\alpha$ -MSH produced a shift in Bax/Bcl-2 ratio toward astrocyte survival

because it increased Bcl-2 expression and also prevented the effect of

LPS/IFN- $\gamma$  on Bax and Bcl-2 expression. In summary, these findings

suggest that  $\alpha$ -MSH, through MC4R activation, attenuates LPS/IFN- $\gamma$ -induced inflammation by decreasing iNOS and COX-2 expression and prevents LPS/IFN- $\gamma$ -induced apoptosis of astrocytes by

modulating the expression of proteins of the Bcl-2 family.

RE.CNT 54 THERE ARE 54 CITED REFERENCES AVAILABLE FOR THIS RECORD  
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L22 ANSWER 2 OF 36 CAPLUS COPYRIGHT 2008 ACS on STN

AN 2007:812134 CAPLUS

DN 148:97655

TI Alpha-fetoprotein-specific transfer factors downregulate alpha-fetoprotein

expression and specifically induce apoptosis in Bel7404 alpha-fetoprotein-positive hepatocarcinoma cells

AU Zhang, Hui; Bai, Zengliang; Chen, Jing; Wang, Ze; Li, Juan

CS School of Life Science, Shandong University, Jinan, Peop. Rep. China

SO Hepatology Research (2007), 37(7), 557-567

CODEN: HPRSFM; ISSN: 1386-6346

PB Blackwell Publishing Asia Pty Ltd.

DT Journal

LA English

AB Aim: To investigate the mechanisms of AFP-specific transfer factors

(AFP-TF) in induced Bel7402 cells apoptosis. Further, we investigate the

interaction between AFP-TF and AFP in the apoptosis. Methods: Bel7402 and

HepG2 AFP-pos. hepatocarcinoma cell lines, SK-Hep-1 AFP-neg. hepatocarcinoma cell line and Changliver normal liver cell line are used. Cell viability is evaluated by MTT assay and apoptosis is measured by Hoechst33342 staining and TUNEL assay. FACS is used to

analyze the cell cycle. AFP expression is examined by RT-PCR, Western

blotting and immunocytochem. The interaction between AFP-TF and AFP in

the apoptosis is investigated by addition of AFP in cultures or AFP

transfection in Bel7402 cells prior to AFP-TF treatment. Mitochondrial

membrane potential ( $\Delta\Psi_m$ ) and intracellular  $\text{Ca}^{2+}$  concentration are resp. measured by Rhodamine123 and Fluo-3 AM Ester. Western blotting detects the involvement of several apoptosis-related proteins.

Finally, caspase-3 and Caspase-9 activity are resp. examined

Results: AFP-TF can induce apoptosis in Bel7402 and HepG2

AFP-pos.

hepatocarcinoma cells, but not SK-Hep-1 and Changliver cells.

AFP-mRNA

level changes little in apoptotic Bel7402 cells; while AFP expression is downregulated and uniformly dispersed throughout the whole cell.

Addition of

exogenous AFP or overexpression of intracellular AFP can reduce such

apoptotic effect. Besides, apoptotic Bel7402 cells show a disruption of

$\Delta\Psi_m$ , an immediate elevation of  $\text{Ca}^{2+}$  concentration, a prominently

decreased ratio of bcl-2 to bax, a release of cytochrome c from mitochondria to cytosol, and ultimately an activation of caspase-9 and

caspase-3. Conclusion: AFP-TF induced Bel7402 cells apoptosis is mitochondrial-dependent and is mediated by the interaction of

AFP-TF with

intracellular AFP.

RE.CNT 28 THERE ARE 28 CITED REFERENCES AVAILABLE FOR THIS RECORD  
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L22 ANSWER 3 OF 36 CAPLUS COPYRIGHT 2008 ACS on STN

AN 2006:1316230 CAPLUS

DN 146:200431

TI ( $\alpha/\beta+\alpha$ )-Peptide Antagonists of BH3 Domain/Bcl-xL

Recognition: Toward General Strategies for Foldamer-Based

Inhibition of

Protein-Protein Interactions

AU Sadowsky, Jack D.; Fairlie, W. Douglas; Hadley, Erik B.; Lee, Hee-Seung;

Umezawa, Naoki; Nikolovska-Coleska, Zaneta; Wang, Shaomeng;

Huang, David

C. S.; Tomita, York; Gellman, Samuel H.

CS Department of Chemistry, University of Wisconsin, Madison, WI, 53706, USA

SO Journal of the American Chemical Society (2007), 129(1), 139-154  
CODEN: JACSAT; ISSN: 0002-7863

PB American Chemical Society

DT Journal

LA English

OS CASREACT 146:200431

AB The development of mols. that bind to specific protein surface sites and

inhibit protein-protein interactions is a fundamental challenge in mol.

recognition. New strategies for approaching this challenge could have important long-term ramifications in biol. and medicine. We are exploring the concept that unnatural oligomers with well-defined conformations ("foldamers") can mimic protein secondary structural elements and thereby block specific protein-protein interactions. Here, we describe the identification and anal. of helical peptide-based foldamers that bind to a specific cleft on the anti-apoptotic protein Bcl-xL by mimicking an  $\alpha$ -helical BH3 domain. Initial studies, employing a fluorescence polarization (FP) competition assay, revealed that among several  $\alpha/\beta$ - and  $\beta$ -peptide foldamer backbones only  $\alpha/\beta$ -peptides intended to adopt 14/15-helical secondary structure display significant binding to Bcl-xL. The most tightly binding Bcl-xL ligands are chimeric oligomers in which an N-terminal  $\alpha/\beta$ -peptide segment is fused to a C-terminal  $\alpha$ -peptide segment ( $(\alpha/\beta+\alpha)$ -peptides). Sequence-affinity relationships were probed via standard and nonstandard techniques (alanine scanning and hydrophile scanning, resp.), and the results allowed us to construct a computational model of the ligand/Bcl-xL complex. Anal. ultracentrifugation with a high-affinity  $(\alpha/\beta+\alpha)$ -peptide established 1:1 ligand:Bcl-xL stoichiometry under FP assay conditions. Binding selectivity studies with the most potent  $(\alpha/\beta+\alpha)$ -peptide, conducted via surface plasmon resonance measurements, revealed that this ligand binds tightly to Bcl-w as well as to Bcl-xL, while binding to Bcl-2 is somewhat weaker. No binding could be detected with Mcl-1. We show that our most potent  $(\alpha/\beta+\alpha)$ -peptide can induce cytochrome C release from mitochondria, an early step in apoptosis, in cell lysates, and that this activity is dependent upon inhibition of protein-protein interactions involving Bcl-xL.

RE.CNT 88      THERE ARE 88 CITED REFERENCES AVAILABLE FOR THIS RECORD  
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L22 ANSWER 4 OF 36 CAPLUS COPYRIGHT 2008 ACS on STN  
AN 2005:1055893 CAPLUS  
DN 143:403736

TI Activation of caspase 8 in the pituitaries of  
streptozotocin-induced  
diabetic rats: Implication in increased apoptosis of lactotrophs

AU Arroba, Ana I.; Frago, Laura M.; Argente, Jesus; Chowen, Julie A.  
CS Hospital Infantil Universitario Nino Jesus, Universidad Autonoma,  
Department of Endocrinology, Madrid, 28009, Spain  
SO Endocrinology (2005), 146(10), 4417-4424  
CODEN: ENDOAO; ISSN: 0013-7227

PB Endocrine Society

DT Journal

LA English

AB Lactotroph cell death is increased in streptozotocin-induced  
diabetic

rats. To determine the mechanism involved, cell death proteins  
were accessed

in pituitaries of diabetic (streptozotocin at 65 mg/kg, 2 mo  
evolution)

and control male rats by Western blot anal. and double  
immunohistochem.

The intact and cleaved forms of caspase 9 were increased in  
diabetic rat

pituitaries compared with controls. Although the proforms of  
caspases 3,

6, and 7 were increased in diabetic rat pituitaries, their  
activated forms

were either unchanged or decreased. Activation of these  
effector caspases

may be blocked by the increased expression of X-chromosome-linked  
inhibitor of apoptosis protein (XIAP) in diabetic rat  
pituitaries.

However, in diabetic rats, XIAP expression in lactotrophs was  
decreased,

suggesting that this cell type is not protected. Caspase 8,  
p53, and

nuclear factor  $\kappa$ B were more highly activated in diabetic rat  
pituitaries, with caspase 8 colocalization in lactotrophs being  
increased.

These results suggest that, in the pituitaries of diabetic rats,  
the

cascades of normal cell turnover are partially inhibited,  
possibly via XIAP, and this may be cell specific. Furthermore,  
activation

of the extrinsic cell-death pathway, including activation of  
caspase 8,

may underlie the diabetes-associated increase in lactotroph  
death.

RE.CNT 56 THERE ARE 56 CITED REFERENCES AVAILABLE FOR THIS RECORD  
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L22 ANSWER 5 OF 36 CAPLUS COPYRIGHT 2008 ACS on STN .

AN 2005:430555 CAPLUS

DN 142:476527

TI  $\alpha$ -Melanocortin and endothelin-1 activate antiapoptotic pathways  
and

reduce DNA damage in human melanocytes

AU Kadekaro, Ana Luisa; Kavanagh, Renny; Kanto, Hiromi; Terzieva, Silva;

Hauser, Jennifer; Kobayashi, Nobuhiko; Schwemberger, Sandy; Cornelius,

James; Babcock, George; Shertzer, Howard G.; Scott, Glynis;

Abdel-Malek,  
Zalfa A.

CS Department of Dermatology, University of Cincinnati College of Medicine

and Shriners' Burns Institute, Cincinnati, OH, USA

SO Cancer Research (2005), 65(10), 4292-4299

CODEN: CNREA8; ISSN: 0008-5472

PB American Association for Cancer Research

DT Journal

LA English

AB UV radiation is an important etiol. factor for skin cancer, including

melanoma. Constitutive pigmentation and the ability to tan are considered the main photoprotective mechanism against sun-induced carcinogenesis. Pigmentation in the skin is conferred by

epidermal

melanocytes that synthesize and transfer melanin to

keratinocytes.

Therefore, insuring the survival and genomic stability of

epidermal

melanocytes is critical for inhibiting photocarcinogenesis,

particularly

melanoma, the most deadly form of skin cancer. The paracrine

factors

$\alpha$ -melanocortin and endothelin-1 are critical for the

melanogenic response of cultured human melanocytes to UV

radiation. The

authors report that  $\alpha$ -melanocortin and endothelin-1 rescued

human

melanocytes from UV radiation-induced apoptosis and reduced DNA

photoproducts and oxidative stress. The survival effects of

$\alpha$ -melanocortin and endothelin-1 were mediated by activation of

the

melanocortin 1 and endothelin receptors, resp. Treatment of

melanocytes

with  $\alpha$ -melanocortin and/or endothelin-1 before exposure to UV

radiation activated the inositol triphosphate kinase-Akt pathway

and

increased the phosphorylation and expression of the

microphthalmia-related

transcription factor. Treatment with  $\alpha$ -melanocortin and/or

endothelin-1 enhanced the repair of cyclobutane pyrimidine

dimers and

reduced the levels of hydrogen peroxide induced by UV radiation.

These

effects are expected to reduce genomic instability and mutagenesis.

RE.CNT 49      THERE ARE 49 CITED REFERENCES AVAILABLE FOR THIS RECORD  
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L22 ANSWER 6 OF 36 CAPLUS COPYRIGHT 2008 ACS on STN

AN 2005:1000002 CAPLUS

DN 143:318603

TI  $\alpha$ -Tocopheryl succinate selectively induces apoptosis in  
neuroblastoma cells: Potential therapy of malignancies of the  
nervous  
system?

AU Swettenham, Emma; Witting, Paul K.; Salvatore, Brian A.; Neuzil,  
Jiri

CS Apoptosis Research Group, School of Medical Science, Griffith  
University,  
Southport, Queensland, Australia

SO Journal of Neurochemistry (2005), 94(5), 1448-1456  
CODEN: JONRA9; ISSN: 0022-3042

PB Blackwell Publishing Ltd.

DT Journal

LA English

AB Vitamin E (VE) analogs, epitomized by  $\alpha$ -tocopheryl succinate  
( $\alpha$ -TOS), are potent inducers of apoptosis and anti-cancer  
agents. Here, we tested their effect on the highly malignant

N-type

neuroblastoma (Nb) cells and their differentiated, neuron-like  
counterparts. Nb cells were highly susceptible to several VE  
analogs,

while differentiated Nb cells were relatively resistant to  
 $\alpha$ -TOS.

The importance of caspase-9 rather than caspase-8, as judged by  
specific  
siRNAs studies, together with the loss of the inner mitochondrial  
potential, suggests that  $\alpha$ -TOS triggers apoptosis in Nb cells  
via

the mitochondrial pathway. Cultured Nb cells were sensitized to  
 $\alpha$ -TOS by pre-treatment with Bcl-2, Bcl-xL or Mcl-1 siRNAs,

while the

malignant cell line was more resistant to the vitamin E analog  
when Bax

was knocked down. In contrast, overexpression of Bcl-2 in Nb  
cells

rendered them more resistant to  $\alpha$ -TOS-induced apoptosis. The  
resistance of differentiated Nb cells to  $\alpha$ -TOS-mediated  
apoptosis

occurred via two modes: first, by up-regulation of the  
anti-apoptotic

Bcl-2 family proteins and second, by accumulation of decreased  
levels of

reactive oxygen species when challenged with  $\alpha$ -TOS. We conclude  
that  $\alpha$ -TOS is highly selective in killing malignant brain cancer  
cells while relatively inert toward differentiated neuronal  
cells, and



that vitamin E analogs may be novel therapeutics for the treatment of

tumors such as neuroblastomas.

RE.CNT 41 THERE ARE 41 CITED REFERENCES AVAILABLE FOR THIS RECORD  
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L22 ANSWER 7 OF 36 CAPLUS COPYRIGHT 2008 ACS on STN

AN 2005:781625 CAPLUS

DN 143:343592

TI  $\alpha 5\beta 1$  Integrin stimulates Bcl-2 expression and cell survival through Akt, focal adhesion kinase, and Ca<sup>2+</sup>/calmodulin-dependent protein kinase IV

AU Lee, Byung-Heon; Ruoslahti, Erkki

CS Department of Biochemistry and Research Institute for Cell & Matrix

Biology, School of Medicine, Kyungpook National University, Taegu,

700-422, S. Korea

SO Journal of Cellular Biochemistry (2005), 95(6), 1214-1223

CODEN: JCEBD5; ISSN: 0730-2312

PB Wiley-Liss, Inc.

DT Journal

LA English

AB CHO cells expressing  $\alpha 5\beta 1$  integrin are more resistant to apoptosis and express more Bcl-2 than the same cells engineered to

express  $\alpha v\beta 1$  or cytoplasmically truncated

$\alpha 5\Delta c\beta 1$  integrin as their main fibronectin receptor. The

Bcl-2 up-regulation by  $\alpha 5\beta 1$  is mediated, at least in part, by

the focal adhesion kinase (FAK) and phosphatidylinositol-3 kinase (PI3K)/Akt pathways. Here, we show that integrin-mediated

activation of

Ca<sup>2+</sup>/calmodulin-dependent protein kinase (CaMK) IV, and the

NF- $\kappa$ B

and CREB transcription factors also enhance the

integrin-dependent

regulation of Bcl-2 expression in the  $\alpha 5\beta 1$  cells. A forkhead

transcription factor, which is inactivated Akt, blocked Bcl-2

expression.

The FAK pathway was found to be defective in both the  $\alpha v\beta 1$  and

$\alpha 5\Delta c\beta 1$  cells. These cell lines differed from one another

in 2 Bcl-2-regulating pathways: adhesion through  $\alpha v\beta 1$  failed to

activate Akt, allowing forkhead to suppress Bcl-2 transcription,

whereas

$\alpha 5\Delta c\beta 1$  did not activate NF- $\kappa$ B and CREB, presumably

because CaMK IV was not activated. Our results indicate that 3

pathways,

the FAK, PI3K/Akt, and CaMK IV mediate the survival-supporting

activity of

$\alpha 5\beta 1$  integrin.

RE.CNT 46 THERE ARE 46 CITED REFERENCES AVAILABLE FOR THIS RECORD

ALL CITATIONS AVAILABLE IN THE RE FORMAT

L22 ANSWER 8 OF 36 BIOSIS COPYRIGHT (c) 2008 The Thomson Corporation on STN  
DUPLICATE 1  
AN 2005:235197 BIOSIS  
DN PREV200510021601  
TI Diagnostic challenge of fetal ontogeny and its application on the ovarian teratomas.  
AU Cho, Nam Hoon [Reprint Author]; Kim, Young Tae; Lee, Ji-Hwan; Song, Chanil; Cho, Sung-Woo; Cho, Sang Ho; Chi, Je Geun  
CS Yonsei Univ, Coll Med, Dept Pathol, Brain Korea 21 Project Med Sci, Shinchon Dong 134, Seoul 120752, South Korea  
SO International Journal of Gynecological Pathology, (APR 2005)  
Vol. 24, No. 2, pp. 173-182.  
ISSN: 0277-1691.  
DT Article  
LA English  
ED Entered STN: 23 Jun 2005  
Last Updated on STN: 23 Jun 2005  
AB Although neuroepithelial tubules (NET) often are a component of immature teratoma (IT), they are not always required for diagnosis. Other somatic elements are sufficient and often verified with immunohistochemical stain. This study was designed to determine the definition of immaturity versus fetal ontogeny, using several molecular markers in IT. It is our contention that IT is equivalent to an embryonic stage less than a fertilization age (FA) of 8 weeks, and a mature teratoma (MT) to a fetal stage later than a FA of 8 weeks, whereas an embryonal carcinoma (Eca) matches a pre-embryonic stage earlier than a FA of 2 weeks. The teratomatous components used as a roadmap to evaluate maturity included: a lobular structure of primitive endodermal tubules (FA 4 14 to 6 weeks), a ventricle-lined cortical plate (FA 9 weeks), a complex papillary choroid plexus (FA 10 weeks), melanin deposition in hair follicles (FA 15 weeks), and the bell stage of odontogenesis (FA 19 weeks). The teratomatous components of 25 resected ovarian solid teratoma samples were compared with fetal ontogeny. For an immunohistochemical analysis, the CD30, CD34, CD99, bcl-

2, alpha-fetoprotein (AFP), and placenta-like alkaline phosphatase (PLAP) were assessed. The AFP and Ki-1 were positive in the embryoid body, which was identified at a FA less than 4 weeks in Eca. The AFP was positive in the primitive endodermal components and some of the squamous epithelium in IT. The CD99 and bcl-2 were selectively stained in the primitive NET, which was detected no later than a FA of 6 weeks. The CD34 and bcl-2 were positive in the immature-taking precartilaginous blastomeres, which proved useful for detecting immature cartilage, corresponding to a FA of 5 to 6 weeks. The ontogeny of IT was found to correspond to the embryonic stage at a FA of 2 to 8 weeks, and CD99, CD34, bcl-2, AFP, CD30, and PLAP could be used as supportive tools to define IT. This new grading system could be more scientific and more reproducible in any spectra of teratoma.

L22 ANSWER 9 OF 36 BIOSIS COPYRIGHT (c) 2008 The Thomson Corporation on STN

AN 2005:12993 BIOSIS

DN PREV200500018187

TI Bcl-2 homodimerization involves two distinct binding surfaces, a topographic arrangement that provides an effective mechanism for Bcl-2 to capture activated Bax.

AU Zhang, Zhi; Lapolla, Suzanne M.; Annis, Matthew G.; Truscott, Mary;

Roberts, G. Jane; Miao, Yiwei; Shao, Yuanlong; Tan, Chibing; Peng, Jun;

Johnson, Arthur E.; Zhang, Xuejun C.; Andrews, David W.; Lin, Jialing

[Reprint Author]

CS Hlth Sci CtrDept Biochem and Mol Biol, Univ Oklahoma, 940 Stanton L Young

Blvd, BMSB 935, POB 26901, Oklahoma City, OK, 73190, USA  
jialing-lin@ouhsc.edu

SO Journal of Biological Chemistry, (October 15 2004) Vol. 279, No. 42, pp.

43920-43928. print.

CODEN: JBCHA3. ISSN: 0021-9258.

DT Article

LA English

ED Entered STN: 22 Dec 2004

Last Updated on STN: 22 Dec 2004

AB The homo- and heterodimerization of Bcl-2 family proteins is important for

transduction and integration of apoptotic signals and control of the permeability of mitochondria and endoplasmic reticulum membranes. Here we mapped the interface of the Bcl-2 homodimer in a cell-free system using site-specific photocross-linking. Bcl-2 homodimer-specific photoadducts were detected from 11 of 17 sites studied. When modeled into the structure of Bcl-2 core, the interface is composed of two distinct surfaces: an acceptor surface that includes the hydrophobic groove made by helices 2 and 8 and the loop connecting helices 4 and 5 and a donor surface that is made by helices 1-4 and the loop connecting helices 2 and 3. The two binding surfaces are on separate faces of the three-dimensional structure, explaining the formation of Bcl-2 homodimers, homo- oligomers, and Bcl-2/Bax hetero-oligomers. We show that in vitro the Bcl-2 dimer can still interact with activated Bax as a larger oligomer. However, formation of a Bax/Bcl-2 heterodimer is favored, since this interaction inhibits Bcl-2 homodimerization. Our data support a simple model mechanism by which Bcl-2 interacts with activated Bax during apoptosis in an effective manner to neutralize the proapoptotic activity of Bax.

L22 ANSWER 10 OF 36 BIOSIS COPYRIGHT (c) 2008 The Thomson Corporation on STN

AN 2005:505777 BIOSIS

DN PREV200510301442

TI BCL-2 alpha in human telomerized corneal epithelial cells.

AU Robertson, D. M. [Reprint Author]; Cavanagh, H. D.; Shay, J. W.; Jester, J. V.

CS Univ Texas, SW Med Ctr, Dallas, TX 75230 USA

SO IOVS, (APR 2004) Vol. 45, No. Suppl. 1, pp. U562.

Meeting Info.: Annual Meeting of the

Association-for-Research-in-Vision-

and-Ophthalmology. Ft Lauderdale, FL, USA. April 24 -29, 2004.

Assoc Res

Vis & Ophthalmol.

CODEN: IOVSDA. ISSN: 0146-0404.

DT Conference; (Meeting)

Conference; (Meeting Poster)

LA English

ED Entered STN: 23 Nov 2005

Last Updated on STN: 23 Nov 2005

AB Purpose: In the human corneal epithelium, the proto-oncogene BCL-2

exhibits a gradient pattern of expression decreasing from limbus to

central cornea and basal to superficial layer, with a loss of expression

in surface epithelial cells prior to desquamation. The purpose of this

experiment is to examine the expression of BCL-2 in a normally differentiating corneal epithelial cell line to validate this cell line as

a viable model for studying surface cell shedding in vitro.

Methods:

Human Telomerized Corneal Epithelial (hTCEpi) cells immortalized with

human telomerase reverse transcriptase were grown on collagen coated culture inserts (Corning) submerged in KGM-2 culture medium (Clonetics) containing 1.15 mM calcium for 7 days. Cells were

then

air-lifted to induce differentiation and examined at day 0, 7 and 10.

Western Blotting using an anti-Keratin K3 antibody (Biogenesis) was used

to assess epithelial differentiation. Levels of Bcl-2 expression were

determined using an anti-BCL-2 monoclonal antibody (Ancell). RT PCR to

generate a 128 bp fragment crossing the intron/exon border of BCL-2 was

used to confirm the protein was splice variant alpha.

Results: Consistent

with previously reported findings, following 7 days of air-lifted culture,

hTCEpi constructs differentiate in vitro similar to the human cornea in

vivo demonstrated by K3 expression. Western Blotting confirmed that the

26 kD BCL-2 protein is "pressed at all time points. Primers specific for

splice variant alpha confirmed that the 26 kD protein was BCL-2 alpha. Conclusions: DISCUSSION: These data suggest that hTCEpi cells express the full length BCL-2 transcript

(splice variant

alpha) containing four conserved homology domains, a regulatory loop, and a

transmembrane domain; and that the BCL-2 protein is expressed in hTCEpi

cell constructs at all stages of differentiation. These findings

are in agreement with previously reported immunohistochemistry demonstrating BCL-2 in both the normal human cornea and our hTCEpi cell line. Taken together, these findings demonstrate a normal pattern of BCL-2 gene expression in the hTCEpi cell line, validating it as a viable model for studying surface cell shedding in vitro.

L22 ANSWER 11 OF 36 BIOSIS COPYRIGHT (c) 2008 The Thomson Corporation on

STN

DUPLICATE 2

AN 2003:555263 BIOSIS

DN PREV200300558218

TI Cycloheximide and actinomycin D delay death and affect bcl-2, bax, and Ice gene expression in astrocytes under in vitro ischemia.

AU Yu, Albert Cheung Hoi [Reprint Author]; Yung, Hon Wa; Hui, Michael Hung

Kit; Lau, Lok Ting; Chen, Xiao Qian; Collins, Richard A.

CS Department of Neurobiology, Neuroscience Research Institute, Peking

University, Peking University Health Science Center, 38 Xue Yuan Road,

Beijing, 100083, China

achy@dnachip.com.hk; achy@bjmu.edu.cn

SO Journal of Neuroscience Research, (October 15 2003) Vol. 74, No. 2, pp.

318-325. print.

ISSN: 0360-4012 (ISSN print).

DT Article

LA English

ED Entered STN: 26 Nov 2003

Last Updated on STN: 26 Nov 2003

AB An in vitro ischemia model was established and the effect of the metabolic

inhibitors cycloheximide (CHX) and actinomycin D (ActD) on apoptosis in

astrocytes under ischemia studied. CHX decreased by 75% the number of

cells dying after 6 hr of ischemia compared with control cultures.

TdT-mediated dUTP nick end labelling (TUNEL) staining of comparable

cultures was reduced by 40%. ActD decreased cell death by 60% compared

with controls. The number of TUNEL-positive cells was reduced by 38%.

The nuclear shrinkage in TUNEL-positive astrocytes in control cultures did

not occur in ActD-treated astrocytes, indicating that nuclear shrinkage

and DNA fragmentation during apoptosis are two unrelated processes. Expression of bcl-2 (alpha and beta), bax, and Ice in astrocytes under similar ischemic conditions, as measured by quantitative reverse transcription-polymerase chain reaction, indicated that ischemia down-regulated bcl-2 (alpha and beta) and bax. Ice was initially down-regulated from 0 to 4 hr, before returning to control levels after 8 hr of ischemia. ActD decreased the expression of these genes. CHX reduced the expression of bcl-2 (alpha and beta) but increased bax and Ice expression. It is hypothesized that the balance of proapoptotic (Bad, Bax) and anti-apoptotic (Bcl-2, Bcl-XI) proteins determines apoptosis. The data suggest that the ratio of Bcl-2/Bad in astrocytes following ActD and CHX treatment does not decrease as much in untreated cells during ischemia. Our data indicate that it is the ratio of Bcl-2 family members that plays a critical role in determining ischemia-induced apoptosis. It is also important to note that ischemia-induced apoptosis involves the regulation of RNA and protein synthesis.

L22 ANSWER 12 OF 36 CAPLUS COPYRIGHT 2008 ACS on STN DUPLICATE 3  
 AN 2002:829670 CAPLUS  
 DN 138:85054

TI Bcl-2 and Porin Follow Different Pathways of TOM-dependent  
 Insertion into  
 the Mitochondrial Outer Membrane

AU Motz, Christian; Martin, Heiko; Krimmer, Thomas; Rassow, Joachim  
 CS Institut für Mikrobiologie, Universität Hohenheim,  
 Stuttgart-Hohenheim,  
 D-70593, Germany

SO Journal of Molecular Biology (2002), 323(4), 729-738  
 CODEN: JMOBAK; ISSN: 0022-2836

PB Elsevier Science Ltd.

DT Journal

LA English

AB The bcl-2 gene encodes a 26 kDa protein which functions as a  
 central

regulator of apoptosis. Here we investigated the pathway of Bcl-2 $\alpha$  into the mitochondrial outer membrane using the yeast *Saccharomyces cerevisiae* as a model organism. We found that

interactions of Bcl-2 $\alpha$  with the  
 mitochondrial import receptor Tom20 are dependent on two pos.

charged lysine residues in the immediate vicinity of the carboxy-terminal

hydrophobic membrane anchor. The targeting function of these residues is

independent of Tom22. Subsequent insertion of Bcl-2.

alpha. into the mitochondrial outer membrane does not require Tom5

or Tom40, indicating that Bcl-2 $\alpha$

bypasses the general import pore (GIP). Bcl-2.

alpha. shows a unique pattern of interactions with the components of the mitochondrial TOM complex, demonstrating that at least two different pathways lead from the import receptor Tom20 into the mitochondrial outer membrane.

RE.CNT 53        THERE ARE 53 CITED REFERENCES AVAILABLE FOR THIS RECORD  
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L22 ANSWER 13 OF 36 BIOSIS COPYRIGHT (c) 2008 The Thomson Corporation on

STN

AN 2002:368762 BIOSIS

DN PREV200200368762

TI Dynamic membrane topology of Bcl-2 during apoptosis.

AU Kim, Peter K. [Reprint author]; Annis, Matthew G. [Reprint author]; Zhu,

Weijia [Reprint author]; Falcone, Mina [Reprint author]; Leber, Brian;

Andrews, David W. [Reprint author]

CS Biochemistry, McMaster University, 1200 Main St West, Hamilton, ON, L8N2Z5, Canada

SO FASEB Journal, (March 20, 2002) Vol. 16, No. 4, pp. A522. print. Meeting Info.: Annual Meeting of the Professional Research Scientists on

Experimental Biology. New Orleans, Louisiana, USA. April 20-24, 2002.

CODEN: FAJOEC. ISSN: 0892-6638.

DT Conference; (Meeting)

Conference; Abstract; (Meeting Abstract)

LA English

ED Entered STN: 3 Jul 2002

Last Updated on STN: 3 Jul 2002

AB Bcl-2 family proteins regulate apoptosis by multiple mechanisms including

the formation of pores. The structure of Bcl-XL resembles that of

diphtheria toxin, a protein capable of forming pores in membranes. This

observation initiated our study into the pore-forming capabilities of

Bcl-2 in culture cells. The alpha5 and alpha6 helices of Bcl-2 are believed to insert into the membrane bilayer to form a pore.

To assess the conformation of Bcl-2, we examined the local environment of



cys158, located in the alpha5 helix near the base of the pore forming region, and cys229, located in the transmembrane domain, using the lipid-impermeant cysteine modifying agent iodoacetylaminostilbene disulfonic acid (IASD). Only cys residues in the lipid bilayer are protected from modification by IASD. We demonstrate that cys158 of Bcl-2 is readily accessible in Rat 1 cells stably expressing wild type Bcl-2, the mitochondrial-specific mutant or the ER-specific mutant. However, upon induction of apoptosis cys158 is protected from modification (and hence integrated into membranes). This is the first in vivo evidence demonstrating the putative pore forming conformation of Bcl-2.

L22 ANSWER 14 OF 36 CAPLUS COPYRIGHT 2008 ACS on STN

AN 2001:369365 CAPLUS

DN 135:316528

TI Protecting the myocardium from ischemic injury: A critical role for

$\alpha$ 1-Adrenoreceptors?

AU Salvi, Sundeep

CS Department of Medicine, Southampton General Hospital, Southampton, SO16 6YD, UK

SO Chest (2001), 119(4), 1242-1249

CODEN: CHETBF; ISSN: 0012-3692

PB American College of Chest Physicians

DT Journal; General Review

LA English

AB A review with 48 refs. Ischemic preconditioning (IPC) refers to the

ability of short periods of ischemia to make the myocardium more resistant

to a subsequent ischemic insult. It is the most powerful form of endogenous protection against myocardial infarction and was demonstrated

in all species evaluated to date. However, the cellular mechanisms that

drive IPC remain poorly understood. This hypothesis describes an important role for  $\alpha$ 1-adrenoreceptors in mediating IPC and discusses

the underlying mechanisms by which this is likely achieved.

$\alpha$ 1-Adrenoreceptors are present in the myocardium of all mammalian species, and several lines of evidence suggest that they play an

important role in mediating IPC. During periods of myocardial

hypoxia/ischemia, cardiomyocytes have to rely solely on anaerobic glycolysis for energy production; for this, the cells have to depend on

increased glucose entry inside the cell as well as increased glycolysis.

Stimulation of  $\alpha 1$ -adrenoreceptors increases glucose transport inside

the cardiomyocytes by translocating glucose transporter (GLUT)-1 and

GLUT-4 from the cytoplasm to the plasma membrane, enhances glycogenolysis

by activating phosphorylase kinase, increases the rate of glycolysis by

activating the enzyme phosphofructokinase, reduces intracellular acidity

produced during excessive glycolysis by activating the  $\text{Na}^+/\text{H}^+$  exchanger,

and inhibits apoptosis by increasing the levels of the antiapoptotic

protein Bcl-2. Myocardial ischemia produces an increase in the expression

of  $\alpha 1$ -adrenoreceptors in cardiomyocytes, as well as increases the

levels of its agonist norepinephrine by several fold. During ischemic

states, upregulation of  $\alpha 1$ -adrenoreceptors and increase in norepinephrine release could be a powerful adaptive mechanism that drives

IPC. An understanding into the role of  $\alpha 1$ -adrenoreceptors in mediating IPC could not only point to newer treatments for limiting

myocardial damage during myocardial infarction or heart surgery, but could

also help in avoiding the use of  $\alpha 1$ -antagonists in patients with ischemic heart disease.

RE.CNT 48 THERE ARE 48 CITED REFERENCES AVAILABLE FOR THIS RECORD  
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L22 ANSWER 15 OF 36 EMBASE COPYRIGHT (c) 2008 Elsevier B.V. All rights

reserved on STN

AN 2002034170 EMBASE

TI BCL2 and BAX mRNA concentration profile in fibrillary astrocytoma.

AU Mazurek, U. (correspondence); Bierzynska-Macyszyn, G.; Gola, J.; Orchel,

J.; Slowinski, J.; Wilczok, T.

CS Dept. Molec. Bio. Biochem/Biopharm., Medical University of Silesia,

Narcyow 1 Street, Sosnowiec, Poland.

umazurek@farmant.slam.katowice.pl

SO Folia Histochemica et Cytobiologica, (2001) Vol. 39, No. SUPPL. 2, pp.

179-180.

Refs: 10

ISSN: 0239-8508 CODEN: FHCYEM

CY Poland

DT Journal; Conference Article; (Conference paper)

FS 014 Radiology

016 Cancer

029 Clinical and Experimental Biochemistry

030 Clinical and Experimental Pharmacology

037 Drug Literature Index

008 Neurology and Neurosurgery

LA English

SL English

ED Entered STN: 7 Feb 2002

Last Updated on STN: 7 Feb 2002

AB A high level of the BCL2 protein and the lack of apoptosis promoting

protein BAX are beginning to be treated as markers of cellular resistance to anti-neoplastic drugs. The object of the study

were

specimens from stereotactic biopsy of astrocytoma fibrillare in the

central brain area, inaccessible to conventional surgery. The cytological

preparations have been evaluated with histopathological and immunohistochemical methods in order to determine the origin of the tumour

and assess cell proliferation activity. The molecular analysis conducted

in order to determine the sensitivity of the tumour to radio- or chemotherapy included the determination of the number of mRNA

BCL2 alpha

and beta molecules and of BAX in 1 µg total RNA obtained from microscope slides. A higher expression of BAX than of

BCL2-alpha is a

prognosis for a positive result of chemo- or radiotherapy. A trace number

of mRNA BCL2-beta molecules and a smaller number of mRNA

BCL2-alpha

molecules than mRNA BAX is a good prognosis for therapy.

L22 ANSWER 16 OF 36 BIOSIS COPYRIGHT (c) 2008 The Thomson Corporation on

STN

DUPLICATE 4

AN 2001:123816 BIOSIS

DN PREV200100123816

TI Effects of phenytoin on glutathione status and oxidative stress biomarker

gene mRNA levels in cultured precision human liver slices.

AU Gallagher, Evan P. [Reprint author]; Sheehy, Karen M.

CS Department of Physiological Sciences and Center for Environmental and

Human Toxicology, University of Florida, Gainesville, FL,  
32611-0885, USA

gallaghere@mail.vetmed.ufl.edu

SO Toxicological Sciences, (January, 2001) Vol. 59, No. 1, pp.  
118-126.

print.

ISSN: 1096-6080.

DT Article

LA English

ED Entered STN: 7 Mar 2001

Last Updated on STN: 15 Feb 2002

AB Cellular production of reactive oxygen species (ROS) has been  
implicated

as an important mechanism of chemical teratogenesis and  
developmental  
toxicity. Unfortunately, the lack of relevant model systems has  
precluded

studies targeting the role of ROS in human teratogenesis and  
prenatal  
toxicity. In the current study, we have used cultured precision  
human

prenatal liver slices to study the effects of the human teratogen  
phenytoin (diphenylhydantoin; Dilantin) on cell toxicity,  
glutathione

redox status, and steady-state mRNA expression of a panel of  
oxidative

stress-related biomarker genes. The biomarker genes analyzed  
were p53,

bcl-2, alpha class glutathione S-transferases  
isozymes A1 and A4 (hGSTA1 and hGSTA4), and the catalytic  
subunit of

gamma-glutamylcysteine synthetase (gammaGCS-HS). Liver slices  
(200  $\mu$ m)

were prepared from second trimester prenatal livers and cultured  
in the

presence of 0, 250  $\mu$ M, and 1000  $\mu$ M phenytoin for 18 h.

Exposure to 1000

$\mu$ M phenytoin elicited 41% and 34% reductions in slice  
intracellular

potassium and reduced glutathione (GSH) concentrations,  
respectively. The

reduction in slice GSH concentrations at 1000  $\mu$ M phenytoin was  
accompanied by a 2.2-fold increase in the percentage of total  
slice

glutathione consisting of GSSG, and a 3.9-fold increase in hGSTA1  
steady-state mRNA expression. Exposure to 250  $\mu$ M or 1000  $\mu$ M  
phenytoin

also elicited a relatively minor (less than 2-fold) but  
significant

increase in p53 steady-state mRNA expression. In contrast, the  
steady-state levels of gammaGCS-HS, hGSTA4, and bcl-2 mRNAs were  
not

affected by phenytoin exposure. Our findings in a relevant human model system are supportive of a protective role of GSH and hGSTA1 against phenytoin toxicity and teratogenesis. These studies also demonstrate the utility of using cultured human prenatal liver slices as a relevant tool for developmental toxicology studies.

L22 ANSWER 17 OF 36 CAPLUS COPYRIGHT 2008 ACS on STN

AN 2000:380163 CAPLUS

DN 133:173639

TI Study of the Secondary Structure of the C-Terminal Domain of the Antiapoptotic Protein Bcl-2 and Its Interaction with Model Membranes

AU Martinez-Senac, Maria del Mar; Corbalan-Garcia, Senena; Gomez-Fernandez, Juan C.

CS Departamento de Bioquimica y Biologia Molecular A Facultad de Veterinaria,

Universidad de Murcia, Murcia, E-30080, Spain

SO Biochemistry (2000), 39(26), 7744-7752

CODEN: BICHAW; ISSN: 0006-2960

PB American Chemical Society

DT Journal

LA English

AB Bcl-2 is a protein which inhibits programmed cell death. It is associated to

many cell membranes such as mitochondrial outer membrane, endoplasmic

reticulum, and nuclear envelope, apparently through a C-terminal hydrophobic domain. We have used IR spectroscopy to study the secondary

structure of a synthetic peptide (a 23mer) with the same sequence as this

C-terminal domain (residues 217-239) of Bcl-2. The spectrum of this

peptide in D2O buffer shows an amide I' band with a maximum at 1622 cm<sup>-1</sup>,

which clearly indicates its tendency to aggregate in aqueous solvent. However,

the peptide incorporated in multilamellar phosphatidylcholine membranes

shows a totally different spectrum of the amide I' band, with a maximum at

1655 cm<sup>-1</sup>, indicating a predominantly  $\alpha$ -helical structure.

Addition of

the peptide to unilamellar vesicles destabilized them and released

encapsulated carboxyfluorescein. Differential scanning calorimetry of

dimyristoylphosphatidylcholine multilamellar vesicles in which the peptide

was incorporated revealed that increasing concns. of the peptide progressively broadened the pretransition and the main transition, as is

to be expected for a membrane integral mol. Fluorescence polarization of

1,6-diphenyl-1,3,5-hexatriene in fluid phosphatidylcholine vesicles showed

that increasing concns. of the peptide produced increased polarization

values, pointing to an increase in the apparent order of the membrane and

indicating that high concns. of the peptide considerably broaden the phase

transition of dimyristoylphosphatidylcholine multilamellar vesicles.

Quenching the intrinsic fluorescence of the Tyr-235 of the peptide, by KI,

indicated that this aminoacyl residue is highly exposed to aqueous solvent

when incorporated in phospholipid vesicles. The results are

discussed in terms of their relevance to the proposed topol. of insertion

of Bcl-2 into biol. membranes.

RE.CNT 80 THERE ARE 80 CITED REFERENCES AVAILABLE FOR THIS RECORD  
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L22 ANSWER 18 OF 36 BIOSIS COPYRIGHT (c) 2008 The Thomson  
Corporation on

STN

DUPLICATE 5

AN 2000:173007 BIOSIS

DN PREV200000173007

TI Gene expressions during the development and sexual  
differentiation of the  
olfactory bulb in rats.

AU Wong, C. C. [Reprint author]; Poon, W. H.; Tsim, T. Y.; Wong,  
Eugene Y.

K.; Leung, M. S.

CS Department of Physiology, Chinese University of Hong Kong,  
Shatin, New

Territories, Hongkong, China

SO Developmental Brain Research, (Feb. 7, 2000) Vol. 119, No. 2,  
pp. 187-194.

print.

CODEN: DBRRDB. ISSN: 0165-3806.

DT Article

LA English

ED Entered STN: 3 May 2000

Last Updated on STN: 4 Jan 2002

AB In this study, expressions of cell-cycle-related genes: p53,  
retinoblastoma (Rb), p21, bcl-2alpha, bcl-2beta; protooncogene  
c-ski;

glial cell marker protein gene S100beta; neurotransmitter gene,  
substance

P and sexual-differentiation-related genes, androgen receptor (AR) and estrogen receptor beta (ERbeta), are studied in the olfactory bulb of groups of both six female and six male rats at the ages of 3, 10, 20 and 40 days. Expressions of housekeeping genes such as beta-actin, cyclophilin and proliferating cell nuclear antigens (PCNA) are determined using reverse transcription polymerase chain reaction (RT-PCR) for the correction of unequal amount of cDNA added into the samples. Using labeled  $^{32}\text{P}$ -dCTP and Phosphorimager technology, relative abundance of radioactivities of the PCR products is obtained by dividing the radioactivity of each individual sample by the corresponding radioactivities of different housekeeping genes. Data evaluated by Two-way ANOVA indicate that only the bcl-2alpha gene expression is affected significantly by age, sex and their interactions no matter which of the three housekeeping genes is used for correction. When beta-actin was used for corrections, effects of age but not sex were found in the expressions of p53, Rb, p21, AR, ERbeta, substance P and S100beta genes, but not in bcl-2beta, c-ski, cyclophilin and PCNA genes. While cyclophilin was used for corrections, only the p53, Rb, AR, ERbeta, substance P and S100beta but not the bcl-2beta, p21, c-ski, PCNA and beta-actin genes are affected by age. They are all not influenced by sex of the animals. Only the AR, ERbeta and S100beta genes are age-dependent when PCNA was used for the correction. The other gene expressions are not altered by sex, while the interactions of age and sex were found to be significantly affecting the bcl-2beta gene expression. Conclusively, developmental changes of the p53, Rb, AR, ERbeta, substance P and S100beta genes expressions are quite evidenced while only the bcl-2alpha gene seems to change significantly during the sexual differentiation of olfactory bulb in rats.

AN 2001:71196 BIOSIS  
 DN PREV200100071196  
 TI Genes expression in the sorted Merkel cells in sinus hair  
 follicles of the  
 rat.  
 AU Leung, M. S. [Reprint author]; Poon, W. H.; Wong, C. C.  
 CS Chinese Univ Hong Kong, Shatin NT, Hong Kong  
 SO Society for Neuroscience Abstracts, (2000) Vol. 26, No. 1-2, pp.  
 Abstract  
 No.-155.4. print.  
 Meeting Info.: 30th Annual Meeting of the Society of  
 Neuroscience. New  
 Orleans, LA, USA. November 04-09, 2000. Society for  
 Neuroscience.  
 ISSN: 0190-5295.  
 DT Conference; (Meeting)  
 Conference; Abstract; (Meeting Abstract)  
 LA English  
 ED Entered STN: 7 Feb 2001  
 Last Updated on STN: 12 Feb 2002  
 AB Merkel cell-neurite complexes are the slowly adapting type II  
 cutaneous mechanoreceptors. They consisted of a cluster of  
 Merkel cells  
 with attachment of adjacent nerve terminals which respond to  
 light touch  
 on the skin. Vibrissal hair on the face of male rats (apprx 200  
 gm) was  
 excised out for the dissection of the ring of Merkel cells from  
 the sinus  
 hair follicle. The samples were loaded with quinarcrine and  
 digested with  
 Dispace to dissociate the cutaneous cells. The fluorescence  
 labeled  
 Merkel cells and controls (no flourescnece) were sorted out with  
 a Coulter  
 Epic Altra flow cytometer into tubes with lysing buffer for  
 subsequent RNA  
 extraction. The total RNA extracted were subjected to reverse  
 transcription to get the cDNA. PCR were then carried out using  
 32P-labeled dCTP and specific primers for the different genes for  
 programmed cell death and cellular signalling. In order to  
 semi-quantitate the relative amount of mRNA for the different  
 neuropeptides found in the Merkel cells, the amount of mRNA for  
 the  
 household gene beta-actin was employed to normalized the results  
 for  
 different target genes. The radioactive labeled PCR products  
 after 8%  
 native polyacrylamide gel electrophoresis were quantified using a  
 phosphorimager. Programmed cell death related genes like  
 caspace-1,  
 caspace3, bcl-x, BAX, BAD, CSR and calcineurin A were expressed  
 in Merkel



and adjacent cutaneous cells; bcl-2alpha, bcl-2beta, NGFI-A and NGFI-B were detected in Merkel cells only. Interestingly NGFI-C was expressed in the control cells only. For the cellular signalling related genes, unlike most of the genes studied, ryanodine receptor type 2 genes was expressed in control cells only.

L22 ANSWER 20 OF 36 CAPLUS COPYRIGHT 2008 ACS on STN

AN 1999:135058 CAPLUS

DN 130:295067

TI Nuclear localization of  $\beta$ -catenin and loss of apical brush border

actin in cystic tubules of bcl-2 -/- mice

AU Sorenson, Christine M.

CS George M. O'Brien Kidney and Urological Diseases Center, Renal Division,

Department of Medicine, Washington University School of Medicine, St.

Louis, MO, 63110, USA

SO American Journal of Physiology (1999), 276(2, Pt. 2), F210-F217  
CODEN: AJPHAP; ISSN: 0002-9513

PB American Physiological Society

DT Journal

LA English

AB Tight regulation of the rates of cell proliferation and apoptosis is critical

for normal nephrogenesis. Nephrogenesis is profoundly affected by the

loss of bcl-2 expression. Bcl-2-deficient (bcl-2 -/-) mice are born with renal hypoplasia and succumb to renal failure secondary to renal

multicystic disease. Cell-cell and cell-matrix interactions impact tissue

architecture by modulating cell proliferation, migration, differentiation,

and apoptosis. E-cadherin mediates calcium-dependent homotypic cell-cell

interactions that are stabilized by its association with catenins and the actin cytoskeleton. The contribution of altered

cell-cell

interactions to renal cystic disease has not been delineated.

Cystic

kidneys from bcl-2 -/- mice displayed nuclear localization of  $\beta$ -catenin and loss of apical brush border actin staining. The protein levels of  $\alpha$ -catenin,  $\beta$ -catenin, actin, and E-cadherin were not altered in cystic kidneys compared with normal kidneys. Therefore, an altered distribution of  $\beta$ -catenin and actin, in

kidneys

from bcl-2 -/- mice, may indicate improper cell-cell interactions

interfering with renal maturation and contributing to renal cyst formation.

RE.CNT 23      THERE ARE 23 CITED REFERENCES AVAILABLE FOR THIS RECORD  
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L22 ANSWER 21 OF 36 CAPLUS COPYRIGHT 2008 ACS on STN DUPLICATE 6

AN 1998:763358 CAPLUS

DN 130:91864

TI Cytoprotection by Bcl-2 requires the pore-forming  $\alpha 5$  and  $\alpha 6$  helixes

AU Matsuyama, Shigemi; Schendel, Sharon L.; Xie, Zhihua; Reed, John C.

CS Burnham Institute, Program on Apoptosis and Cell Death Research, La Jolla, CA, 92037, USA

SO Journal of Biological Chemistry (1998), 273(47), 30995-31001  
CODEN: JBCHA3; ISSN: 0021-9258

PB American Society for Biochemistry and Molecular Biology

DT Journal

LA English

AB We explored whether the putative channel-forming fifth and sixth  $\alpha$ -helixes of Bcl-2 and Bax account for Bcl-2-mediated cell survival

and Bax-induced cell death in mammalian cells and in the yeast *Saccharomyces cerevisiae*. When  $\alpha 5$ - $\alpha 6$  were either deleted or swapped with each other, the Bcl-2 $\Delta\alpha 5\alpha 6$  deletion mutant and Bcl-2-Bax( $\alpha 5\alpha 6$ ) chimeric protein failed to block apoptosis induced by either Bax or staurosporine in human cells and were unable to

prevent Bax-induced cell death in yeast, implying that the  $\alpha 5$ - $\alpha 6$  region of Bcl-2 is essential for its cytoprotective function. Addnl. expts. indicated that, although  $\alpha 5$ - $\alpha 6$  is necessary, it is also insufficient for the anti-apoptotic activity of

Bcl-2. In contrast, deletion or substitution of  $\alpha 5$ - $\alpha 6$  in Bax reduced but did not abrogate apoptosis induction in human cells, whereas

it did completely nullify cytotoxic activity in yeast, implying that the

pore-forming segments of Bax are critical for conferring a lethal phenotype in yeast but not necessarily in human cells.

Bax $\Delta\alpha 5\alpha 6$  and Bax-Bcl-2(.

$\alpha 5\alpha 6$ ) also retained the ability to dimerize with Bcl-2.

Bax therefore may have redundant mechanisms for inducing apoptosis in

mammalian cells, based on its ability to form  $\alpha 5$ - $\alpha 6$ -dependent channels in membranes and to dimerize with and antagonize anti-apoptotic

proteins such as Bcl-2.

RE.CNT 41      THERE ARE 41 CITED REFERENCES AVAILABLE FOR THIS RECORD  
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L22 ANSWER 22 OF 36 CAPLUS COPYRIGHT 2008 ACS on STN DUPLICATE 7  
 AN 1998:54978 CAPLUS  
 DN 128:178931  
 OREF 128:35275a,35278a  
 TI Alteration of proteins regulating apoptosis, Bcl-2, Bcl-x, Bax, Bak, Bad, ICH-1 and CPP32, in Alzheimer's disease  
 AU Kitamura, Yoshihisa; Shimohama, Shun; Kamoshima, Wataru; Ota, Takashi; Matsuoka, Yasuji; Nomura, Yasuyuki; Smith, Mark A.; Perry, George; Whitehouse, Peter J.; Taniguchi, Takashi  
 CS Department of Neurobiology, Kyoto Pharmaceutical University, Kyoto, Japan  
 SO Brain Research (1998), 780(2), 260-269  
 CODEN: BRREAP; ISSN: 0006-8993  
 PB Elsevier Science B.V.  
 DT Journal  
 LA English  
 AB Recently, apoptosis has been implicated in the selective neuronal loss of Alzheimer's disease (AD). Apoptosis is regulated by the B cell leukemia-2 gene product (Bcl-2) family (Bcl-2, Bcl-x, Bax, Bak and Bad) and the caspase family (ICH-1 and CPP32), with apoptosis being prevented by Bcl-2 and Bcl-x, and promoted by Bax, Bak, Bad, ICH-1 and CPP32. In the present study, we examined the levels of these proteins in the membranous and cytosolic fractions of temporal cortex in AD and control brain. In the membranous fraction, the levels of Bcl-2.alpha., Bcl-xL, Bcl-x $\beta$ , Bak and Bad were increased in AD. In the cytosolic fractions, the level of Bcl-x $\beta$  was increased, while Bcl-xL, Bax, Bak, Bad and ICH-1L were unchanged. CPP32 was not detected in AD or control brain. These findings demonstrate a differential involvement of cell death-regulatory proteins in AD and suggest that Bak, Bad, Bcl-2 and Bcl-x are upregulated in AD brains.  
 RE.CNT 68 THERE ARE 68 CITED REFERENCES AVAILABLE FOR THIS RECORD  
 ALL CITATIONS AVAILABLE IN THE RE FORMAT

L22 ANSWER 23 OF 36 CAPLUS COPYRIGHT 2008 ACS on STN  
 AN 1997:346522 CAPLUS  
 DN 127:93998  
 OREF 127:18073a,18076a  
 TI Analysis of a sequenced cDNA library from multiple sclerosis lesions

AU Becker, Kevin G.; Mattson, David H.; Powers, James M.; Gado, Ameer M.;

Biddison, William E.

CS Molecular Immunology Section, Neuroimmunology Branch, National Institute

of Neurological Disorders and Stroke, National Institutes of Health,

Bethesda MD, USA

SO Journal of Neuroimmunology (1997), 77(1), 27-38

CODEN: JNRIDW; ISSN: 0165-5728

PB Elsevier

DT Journal

LA English

AB To identify genes that are expressed in MS pathogenesis, the authors have analyzed a normalized cDNA library made from mRNA obtained

from CNS lesions of a patient with primary progressive MS.

Complementary

DNA clones obtained from this library were subjected to automated DNA

sequencing to generate expressed sequence tags. Anal. of this MS cDNA

library revealed the presence of 54 cDNAs that were associated with immune

activation and indicated the presence of an ongoing inflammatory response

with evidence of both cell-mediated and humoral immune responses. The

surprising finding was that 16 of the cDNAs encoded autoantigens associated

with seven other autoimmune disorders, while only three of these 16

autoantigen cDNAs were present in a similarly constructed adult brain

library. Such aberrant autoantigen expression could provide a source of

secondary autoimmune stimulation that could contribute to the ongoing

inflammatory response in MS. In addition, two cDNAs were found that mapped

to a known MS susceptibility locus (5p14-p12): one encoded an excitatory

amino acid transporter and the other a human homolog of the Drosophila

disabled gene. This approach to the mol. biol. of MS pathogenesis may

help to illuminate previously unappreciated aspects of this disease.

L22 ANSWER 24 OF 36 EMBASE COPYRIGHT (c) 2008 Elsevier B.V. All rights

reserved on STN

AN 1996274872 EMBASE  
 TI [The expanding Bcl2 gene family: Towards a comprehensive approach of the structure/activity relationship of proteins].  
 L'expansion continue de la famille Bcl2. Vers une approche raisonnee des relations structure/activite?.

AU Larsen, C.-J. (correspondence)  
 CS INSERM U 301, Institut de Genetique Moleculaire, 27, Rue Juliette-Dodu,  
 75010 Paris, France.

SO Hematologie, (1996) Vol. 2, No. 4, pp. 301-311.  
 ISSN: 1264-7527 CODEN: HEMAF2

CY France  
 DT Journal; General Review; (Review)  
 FS 016 Cancer  
 022 Human Genetics  
 025 Hematology

LA French  
 SL French; English  
 ED Entered STN: 15 Oct 1996  
 Last Updated on STN: 15 Oct 1996

AB bcl2 gene is the most representative member of a growing family of genes which counts among the main regulators of programmed cell death or apoptosis. Some of the protein members of the family (bcl-2 $\alpha$ , bcl-x(L)) inhibit the cell death process (subfamily 1), whereas others (bax, bak, bik) promote apoptosis (subfamily 2). These functions appear to be carried out through heterodimerization, between members of each subfamily. Numerous works have shown that two highly conserved domains (BH1 and BH2) are needed for heterodimerization and for biological activity. In this review, recent data are presented on the presence of other conserved domains (BH3, NH1, NH2) that appear to be necessary for heterodimerization between members of the BCL2 family as well as for interactions with other cellular proteins. The implication of these new features in the physiopathology of programmed cell death in hematopoiesis and hematopoietical malignancies, is discussed.

L22 ANSWER 25 OF 36 CAPLUS COPYRIGHT 2008 ACS on STN  
 AN 1995:652012 CAPLUS  
 DN 123:80240  
 OREF 123:14247a,14250a

TI The  $\alpha 5 \beta 1$  integrin supports survival of cells on fibronectin and up-regulates Bcl-2 expression  
 AU Zhang, Zhuohua; Vuori, Kristiina; Reed, John C.; Ruoslahti, Erkki  
 CS Cancer Res. Cent., La Jolla Cancer Res. Foundation, La Jolla, CA, 92037, USA  
 SO Proceedings of the National Academy of Sciences of the United States of America (1995), 92(13), 6161-5  
 CODEN: PNASA6; ISSN: 0027-8424  
 PB National Academy of Sciences  
 DT Journal  
 LA English  
 AB Anchorage-dependent cells that are prevented from attaching to an extracellular matrix substrate stop proliferating and may undergo apoptosis. Cell adhesion to a substrate is mediated by the integrin family of cell surface receptors, which are known to elicit intracellular signals upon cell adhesion. We show here that Chinese hamster ovary cells expressing the  $\alpha 5 \beta 1$  integrin, which is a fibronectin receptor, do not undergo apoptosis upon serum withdrawal when the cells are plated on fibronectin. However, the  $\alpha v \beta 1$  integrin, which is also a fibronectin receptor and binds fibronectin on the same RGD motif as  $\alpha 5 \beta 1$ , did not prevent apoptosis on fibronectin of the same cells. The cytoplasmic domain of the integrin  $\alpha 5$  subunit was required for the  $\alpha 5 \beta 1$ -mediated cell survival on fibronectin. The fibronectin-mediated survival effect appeared to be independent of the level of tyrosine phosphorylation of the focal adhesion kinase, which is induced by integrin-mediated cell attachment. The expression of the Bcl-2 protein, which counteracts apoptosis, was elevated in cells attaching to fibronectin through  $\alpha 5 \beta 1$ ; cells attaching through  $\alpha v \beta 1$  survived only if exogenous Bcl-2 was provided. Thus,  $\alpha 5 \beta 1$ , but not the closely related  $\alpha v \beta 1$  integrin, appears to suppress apoptotic cell death through the Bcl-2 pathway.

L22 ANSWER 26 OF 36 BIOSIS COPYRIGHT (c) 2008 The Thomson Corporation on

STN

DUPLICATE 8

AN 1994:299652 BIOSIS

DN PREV199497312652

TI Targeted disruption of Bcl-2-alpha-beta in mice: Occurrence of gray hair, polycystic disease, and lymphocytopenia.

AU Nakayama, Keiko; Nakayama, Kei-Ichi; Negishi, Izumi; Kuida, Keisuke; Sawa,

Hirofumi; Loh, Dennis Y.  
 CS Howard Hughes Med. Inst., Dep. Med. Genetics, Washington  
 University Sch.  
 Med., St. Louis, MO 63110, USA  
 SO Proceedings of the National Academy of Sciences of the United  
 States of  
 America, (1994) Vol. 91, No. 9, pp. 3700-3704.  
 CODEN: PNASA6. ISSN: 0027-8424.  
 DT Article  
 LA English  
 ED Entered STN: 13 Jul 1994  
 Last Updated on STN: 14 Jul 1994  
 AB Mice carrying ablated coding regions of the bcl-2-  
 alpha and bcl-2-beta transcripts have been made. bcl-2-/- mutants  
 are smaller but viable, although about half of them die by 6  
 weeks  
 of age. As shown earlier with somatic bcl-2 gene-targeted mice,  
 the  
 number of lymphocytes markedly decreased within few weeks after  
 birth  
 while other hematopoietic lineages remained unaffected. Among  
 lymphocytes, CD8+ T cells disappeared most quickly followed by  
 CD4+ T  
 cells, whereas B cells were least affected. bcl-2-/-  
 lymphocytes, however,  
 could respond normally to various stimuli including anti-CD3,  
 Con A,  
 phorbol 12-myristate 13-acetate plus ionomycin, interleukin 2,  
 lipopolysaccharide, and anti-IgM antibody. Abnormalities among  
 nonlymphoid organs include smaller auricles, hair color turning  
 gray at  
 4-5 weeks of age, and polycystic kidney disease-like change of  
 renal  
 tubules. These results suggest that Bcl-2 may be involved during  
 morphogenesis where inductive interactions between epithelium and  
 mesenchyme are important such as in the kidneys, hair follicles,  
 and perichondrium of auricles. Surprisingly, the nervous system,  
 intestines, and skin appear normal despite the fact that these  
 organs show  
 high levels of endogeneous Bcl-2 expression in normal mice.

L22 ANSWER 27 OF 36 BIOSIS COPYRIGHT (c) 2008 The Thomson  
 Corporation on  
 STN  
 DUPLICATE 9  
 AN 1994:446674 BIOSIS  
 DN PREV199497459674  
 TI The protein bcl-2-alpha does not require  
 membrane attachment, but two conserved domains to suppress  
 apoptosis.  
 AU Borner, Christoph; Martinou, Isabelle; Mattmann, Chantal;  
 Irmeler, Martin;  
 Schaerer, Esther; Martinou, Jean-Claude; Tschopp, Juerg [Reprint  
 author]

CS Inst. Biochem., Chemin des Boveresses 155, CH-1066 Epalinges, Switzerland

SO Journal of Cell Biology, (1994) Vol. 126, No. 4, pp. 1059-1068. CODEN: JCLBA3. ISSN: 0021-9525.

DT Article

LA English

ED Entered STN: 24 Oct 1994  
Last Updated on STN: 24 Oct 1994

AB Bcl-2 is a mitochondrial- and perinuclear-associated protein that prolongs the lifespan of a variety of cell types by interfering with programmed cell death (apoptosis). Bcl-2 seems to function in an antioxidant pathway, and it is believed that membrane attachment mediated by a COOH-terminal hydrophobic tail is required for its full activity. To identify critical regions in bcl-2-alpha for subcellular localization, activity, and/or interaction with other proteins, we created, by site-directed mutagenesis, various deletion, truncation, and point mutations. We show here that membrane attachment is not required for the survival activity of bcl-2-alpha. A truncation mutant of bcl-2-alpha lacking the last 33 amino acids (T3.1) including the hydrophobic COOH terminus shows full activity in blocking apoptosis of nerve growth factor-deprived sympathetic neurons or TNF-alpha-treated L929 fibroblasts. Confocal microscopy reveals that the T3 mutant departs into the extremities of neurites in neurons and filopodias in fibroblasts. Consistently, T3 is predominantly detected in the soluble fraction by Western blotting, and is not inserted into microsomes after in vitro transcription/translation. We further provide evidence for motifs (S-N and S-II) at the NH-2 and COOH terminus of bcl-2, which are crucial for its activity.

L22 ANSWER 28 OF 36 BIOSIS COPYRIGHT (c) 2008 The Thomson Corporation on

STN

DUPLICATE 10

AN 1995:342154 BIOSIS

DN PREV199598356454

TI Dissection of functional domains in Bcl-2-alpha by site-directed mutagenesis.

AU Borner, Christoph [Reprint author]; Olivier, Reynald; Martinou, Isabelle;



Martinou, Jean-Claude  
CS Inst. Biochem., Univ. Fribourg, Rue du Musee 5, Perolles, CH-1700  
Fribourg, Switzerland  
SO Biochemistry and Cell Biology, (1994) Vol. 72, No. 11-12, pp.  
463-469.

CODEN: BCBIEQ. ISSN: 0829-8211.

DT Article

LA English

ED Entered STN: 10 Aug 1995

Last Updated on STN: 10 Aug 1995

AB Bcl-2-alpha is a mitochondrial or  
perinuclear-associated oncoprotein that prolongs the life span  
of a  
variety of cell types by interfering with programmed cell death.

How

Bcl-2 confers cell survival is unknown, although antioxidant and  
antiprotease functions have been proposed. In addition, protein  
structures of Bcl-2 that are crucial for its survival activity  
are still ill-defined. Bcl-2 can occur as Bcl-2  
-alpha or Bcl-2-beta, two alternatively spliced forms which  
solely differ in their carboxyl termini. The finding that Bcl-  
2-alpha is active and membrane bound, but Bcl-2-beta is  
inactive and cytosolic, indicates that the carboxyl terminus  
contributes

to the survival activity of Bcl-2. This region contains two  
subdomains, a

domain X with unknown function and a hydrophobic stretch  
reported to

mediate membrane association of Bcl-2-alpha.

Recently Bcl-2-related proteins have been identified. These  
include Bax

that heterodimerizes with Bcl-2 and, when overexpressed,  
counteracts Bcl-2.

Bax contains two highly conserved regions of sequence homology  
with Bcl-2,

referred to as Bcl-2 homology 1 and 2 (BH1 and BH2) domains.

Site-directed mutagenesis studies have revealed that both domains  
are not only novel dimerization motifs for the interaction of Bax  
with Bcl-2 but also crucial for the survival activity of Bcl-2.

Interestingly, the C-terminal end of BH2 encompasses the Bcl-  
2-alpha/beta splice site, as well as part of domain X in  
Bcl-2-alpha. To better define the role of

domain X and the hydrophobic C-terminal stretch of Bcl-2  
-alpha for its survival activity, we created various deletion  
and truncation mutations in these regions by site-directed

mutagenesis.

We show here that membrane attachment and therefore the  
hydrophobic

stretch is not required for the survival activity of Bcl-2, but  
part of

domain X appears to be indispensable.

L22 ANSWER 29 OF 36 BIOSIS COPYRIGHT (c) 2008 The Thomson  
Corporation on

STN

DUPLICATE 11

AN 1995:124497 BIOSIS

DN PREV199598138797

TI The BCL2 gene is the prototype of a gene family that controls  
programmed

cell death (apoptosis).

AU Larsen, C.-J

CS INSERM U-301 SDI 159541 CNRS, Inst. Genetique Moleculaire, 27  
rue J. Dodu,

75010 Paris, France

SO Annales de Genetique, (1994) Vol. 37, No. 3, pp. 121-134.

CODEN: AGTQAH. ISSN: 0003-3995.

DT Article

General Review; (Literature Review)

LA French

ED Entered STN: 29 Mar 1995

Last Updated on STN: 29 Mar 1995

AB The BCL2 gene is the most representative member of a family of  
genes that

control cell homeostatic processes in the course of the  
developmental and

adult life. Some members of the BCL2 family (bcl-2-

alpha, bcl-x-L) inhibit apoptosis, whereas some others (Bax,

Bclx-s) induce it. The biological activity of these proteins is

dictated

by: 1) their capacity to be integrated in specific membranes of  
the

cytoplasm; 2) their ability to homo- or heterodimerize, due to  
the

presence of two highly conserved domains which are a signature  
of this gene family. The bcl-2 protein exhibits two main

biochemical

properties: it acts in an antioxidant metabolic pathway aimed at  
eliminating oxygen free radicals that induce lesions in DNA,

lipids and

proteins; it modulates intracellular Ca++ fluxes. BCL2 (and  
presumably

its congeners) interplay with other genes involved in the tight  
control of

cell proliferation and programmed cell death (c-myc, p53). A  
more

comprehensive view of BCL2 functions should benefit to cancer  
chemotherapy

by improving rational approach of the antitumor drug mechanisms.

L22 ANSWER 30 OF 36 BIOSIS COPYRIGHT (c) 2008 The Thomson  
Corporation on

STN

DUPLICATE 12

AN 1994:127756 BIOSIS

DN PREV199497140756

TI Developmental regulation of bcl-2 expression in the thymus.  
AU Moore, N. C. [Reprint author]; Anderson, G.; Williams, G. T.;  
Owen, J. J.  
T.; Jenkinson, E. J.  
CS Centre Clinical Res. Immunology Signalling, Med. Sch., Univ.  
Birmingham,  
Birmingham B15 2TT, UK  
SO Immunology, (1994) Vol. 81, No. 1, pp. 115-119.  
CODEN: IMMUAM. ISSN: 0019-2805.  
DT Article  
LA English  
ED Entered STN: 24 Mar 1994  
Last Updated on STN: 24 Mar 1994  
AB An important factor in shaping the T-cell receptor (TcR)  
repertoire during  
thymocyte development is the susceptibility of double-positive  
(CD4+ CD8+)  
thymocytes to induction of apoptosis (negative selection) when  
the TcR is  
engaged by 'self'-antigens. Recent evidence has suggested that  
this  
susceptibility to apoptosis may be influenced by the expression  
of bcl-2,  
a proto-oncogene known to increase the resistance to apoptosis  
in various  
cell systems. Using a semi-quantitative polymerase chain  
reaction (PCR)  
technique in conjunction with staged embryonic material and  
purified  
thymocyte subpopulations we have investigated patterns of bcl-2  
expression  
during normal T-cell development. Our results show that while  
bcl  
-2-alpha gene expression is readily detectable in  
immature CD3- CD4- CD8- thymocytes and in mature single-positive  
TcR-hi  
cells, it is drastically reduced in TcR negative double-positive  
(CD3-  
CD4+ CD8+) cortical thymocytes of intermediate maturity.  
Careful mapping  
of bcl-2-alpha re-expression in relation to  
the onset of TcR expression within the population of embryonic  
thymocytes  
indicates that bcl-2-alpha is up-regulated  
as soon as TcR molecules are expressed on the surface of CD4+  
CD8+ thymocytes. Therefore, thymocytes susceptible to apoptosis  
on TcR  
ligation express bcl-2-alpha mRNA suggesting  
that changing levels of bcl-2 expression are unlikely to be the  
only determinant regulating susceptibility to apoptosis in the  
thymus.  
The possible implications of these changes in bcl-2 expression  
regarding

other facets of thymocyte development will be discussed.

L22 ANSWER 31 OF 36 CAPLUS COPYRIGHT 2008 ACS on STN

AN 1990:402214 CAPLUS

DN 113:2214

OREF 113:447a,450a

TI Charge configurations in oncogene products and transforming proteins

AU Karlin, Samuel; Brendel, Volker

CS Dep. Math., Stanford Univ., Stanford, CA, 94305, USA

SO Oncogene (1990), 5(1), 85-95

CODEN: ONCNES; ISSN: 0950-9232

DT Journal

LA English

AB Statistically significant charge clusters are of infrequent occurrence in all kinds of proteins. In the 6 standard classes of

protooncogene products, all of the nuclear class contain a significant

charge cluster and several, but not all, of the transmembrane class do,

whereas significant charge clusters or patterns are not found in protooncogenes of primarily cytoplasmic location, nor in membrane-bound

(src-like) protooncogenes, nor in those of the ras family.

Among nuclear

oncogene families, such as myc-, jun-, fos-, myb-, or ets-related, and

among homologous proteins across species, the significant charge clusters

are part of the most conserved region. These gene families generally have similar charge distributions embodying a significant charge

cluster, not of an invariant sign, preceded by a substantial uncharged

stretch of predominantly polar residues. Nuclear transforming proteins

p53 and p68 also contain significant charge clusters together with long

uncharged segments, suggestive of a modular structure of these proteins.

Transmembrane oncogene c-mas contains a mixed charge cluster and c-fms

displays an unusual (0, +)7 pattern, in both cases positioned within their

intracellular activating domain. Distinctive charge configurations for

excreted protooncogenes are of a mixed character. Possible functions, mechanisms, and associated exptl. procedures for studying proteins

with anomalous charge distributions are discussed.

L22 ANSWER 32 OF 36 EMBASE COPYRIGHT (c) 2008 Elsevier B.V. All rights

reserved on STN

AN 1989273433 EMBASE

TI Stress-resistance conferred by high level of bcl-2.  
alpha. protein in human B lymphoblastoid cell.

AU Tsujimoto, Y.

CS The Wistar Institute of Anatomy and Biology, Philadelphia, PA  
19104,

United States.

SO Oncogene, (1989) Vol. 4, No. 11, pp. 1331-1336.

ISSN: 0950-9232 CODEN: ONCNES

CY United Kingdom

DT Journal; Article

FS 025 Hematology

029 Clinical and Experimental Biochemistry

LA English

SL English

ED Entered STN: 12 Dec 1991

Last Updated on STN: 12 Dec 1991

AB High levels of human bcl-2 protein(s) result in (i) the  
tumorigenic

conversion of mouse NIH3T3 cells, (ii) the better survival of  
mouse

myeloid cells in the absence of the required growth factor and  
(iii) give

a growth advantage to human EBV-lymphoblastoid B cells both in  
low serum

medium and limiting dilutions. The effect of the high levels of  
bcl-2

protein in EBV-B cells was further investigated. This revealed  
that high

levels of bcl-2 $\alpha$  protein made EBV-B

cells more resistant to a variety of stresses including the  
application of

heat shock, ethanol, methotrexate and the absence of serum.

Stress

resistance was not observed in EBV-B cells with elevated level  
of c-myc

protein. The mechanism of stress resistance conferred by the bcl  
-2 $\alpha$  protein is yet to be determined although the

resistance does not seem to be the result of an increase in

major heat

shock proteins, hsp70 and hsp90, nor the arrest of cells in

G(1)/G(0)

phase. The increased viability was observed in control

transfectants but

not in bcl-2 transfectants when cells are seeded at higher

density in the absence of serum. Thus the improved survival of

cells as a

result of high levels of the bcl-2 $\alpha$

protein is not specific to the absence of growth factor but is  
found to

occur with a variety of stresses.

L22 ANSWER 33 OF 36 CAPLUS COPYRIGHT 2008 ACS on STN

AN 1988:566863 CAPLUS

DN 109:166863

OREF 109:27599a,27602a

TI Diagnostic methods for detecting human lymphomas associated with chromosome 14 and 18 translocations and cloning, expression, and nucleotide sequence of human bcl-2 gene

IN Tsujimoto, Yoshihide; Croce, Carlos M.

PA Wistar Corp., USA

SO Eur. Pat. Appl., 23 pp.

CODEN: EPXXDW

DT Patent

LA English

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.
DATE	-----	----	-----	-----
-----				
PI	EP 252685	A2	19880113	EP 1987-305863
19870702				
	EP 252685	A3	19900711	
	EP 252685	B1	19930616	
	R: AT, BE, CH, DE, ES, FR, GB, GR, IT, LI, LU, NL, SE			
	US 5015568	A	19910514	US 1986-883687
19860709				
	AT 90792	T	19930715	AT 1987-305863
19870702				
	ES 2003064	T3	19940901	ES 1987-305863
19870702				
	AU 8775328	A	19880218	AU 1987-75328
19870708				
	AU 602704	B2	19901025	
	CA 1340827	C	19991123	CA 1987-541606
19870708				
	JP 63100379	A	19880502	JP 1987-172023
19870709				
	US 5202429	A	19930413	US 1991-663010
19910319				
	US 5595869	A	19970121	US 1992-994941
19921223				
	US 5459251	A	19951017	US 1994-228704
19940418				
	US 5506344	A	19960409	US 1995-435193
19950505				
	US 5523393	A	19960604	US 1995-435181
19950505				
PRAI	US 1986-883687	A	19860709	
	EP 1987-305863	A	19870702	
	US 1991-633010	A1	19910319	
	US 1991-663010	A1	19910319	

US 1992-994941            A1        19921223  
US 1994-228704            A3        19940418

AB    Assays are provided for detecting a class of B-cell neoplasms associated with a chromosome translocation between chromosomes 14 and 18

which is involved in a majority of human follicular lymphomas.

One assay

uses an antibody immunoreactive with a protein overexpressed due to the

chromosome translocation. Another assay involves measurement of the amount

of mRNA which hybridizes to the gene proximal to the translocation

breakpoint. The sequences of the protein-encoding regions of the bcl-2

gene are provided as well as bacterial clones which produce the proteins. A cDNA library from poly(A)+ mRNA of the pre-B-cell leukemia

line 380 was constructed and cloned into  $\lambda$ gt11 phage vectors, and

recombinant clones were screened with a DNA probe consisting of a segment

of chromosome 18 which spans the hotspot of breakpoints of the translocation of chromosome 18 to chromosome 14. Three

independent but

overlapping cDNA clones were obtained. The nucleotide sequences of both

strands of the 5.5- and 3.5-kilobase transcripts were determined

The DNA

sequence of 5105 base pairs of the former reveals one possible open

reading frame of 239 amino acid residues (bcl-2-

alpha.). The latter transcript codes for a 205-amino-acid residue

protein (bcl-2 $\beta$ ), differing from bcl-2.

alpha. protein at the C-terminus.

L22    ANSWER 34 OF 36    EMBASE    COPYRIGHT (c) 2008 Elsevier B.V. All rights

reserved on STN

AN    1988264412    EMBASE

TI    Oncogenic potential of bcl-2 demonstrated by gene transfer.

AU    Reed, J.C.; Cuddy, M.; Slabiak, T.; Croce, C.M.; Nowell, P.C.

CS    Department of Pathology and Laboratory Medicine, University of Pennsylvania School of Medicine, Philadelphia, PA 19104-6082, United

States.

SO    Nature, (1988) Vol. 336, No. 6196, pp. 259-261.

ISSN: 0028-0836    CODEN: NATUAS

CY    United Kingdom

DT    Journal; Article

FS    016        Cancer

LA English  
SL English  
ED Entered STN: 11 Dec 1991  
Last Updated on STN: 11 Dec 1991  
AB Follicular lymphoma is the most common human B-cell malignancy in the United States and Western Europe. Most of the tumours contain t(14;18) chromosome translocations involving the human bcl-2 gene. Translocation of bcl-2 sequences from chromosome 18 into the transcriptionally active immunoglobulin locus at chromosome band 14q32 in B cells deregulates bcl-2 gene expression, resulting in the accumulation of high levels of bcl-2 messenger. Human bcl-2 transcripts generate two proteins, p26 bcl-2- $\alpha$  and p22 bcl-2- $\beta$ , by virtue of alternative splice-site selection. Both proteins have in common their first 196 NH(2)-terminal aminoacids but share little similarity with other sequences in a data bank. Although the biological and biochemical functions of bcl-2 are unknown, recent subcellular localization studies indicate that p26 bcl-2- $\alpha$  associates with cellular membranes, consistent with a stretch of hydrophobic amino acids in its carboxy terminus. The bcl-2 gene may represent a novel oncogene having no known retroviral counterpart. Here we demonstrate the oncogenic potential of bcl-2 through a gene transfer approach.

L22 ANSWER 35 OF 36 BIOSIS COPYRIGHT (c) 2008 The Thomson Corporation on

STN

DUPLICATE 13

AN 1986:437567 BIOSIS

DN PREV198682103755; BA82:103755

TI ANALYSIS OF THE STRUCTURE TRANSCRIPTS AND PROTEIN PRODUCTS OF BCL-2 THE

GENE INVOLVED IN HUMAN FOLLICULAR LYMPHOMA.

AU TSUJIMOTO Y [Reprint author]; CROCE C M

CS WISTAR INST, 3601 SPRUCE ST, PHILADELPHIA, PA 19104, USA

SO Proceedings of the National Academy of Sciences of the United States of

America, (1986) Vol. 83, No. 14, pp. 5214-5218.

CODEN: PNASA6. ISSN: 0027-8424.

DT Article

FS BA



LA ENGLISH  
ED Entered STN: 8 Nov 1986  
Last Updated on STN: 8 Nov 1986  
AB We have determined that the bcl-2 (B-cell leukemia/lymphoma 2) gene is transcribed into three overlapping mRNAs, and we have cloned bcl-2 cDNA sequences. Sequence analysis of the bcl-2 cDNA clones and comparison of their sequences to their genomic counterparts indicate that the bcl-2 gene contains at least two exons. The three bcl-2 transcripts, which are 8.5, 5.5, and 3.5 kilobases (kb) long, overlap within the first exon, but only the 8.5-kb and 5.5-kb transcripts contain sequences of the second exon. The 8.5-kb and 5.5-kb transcripts seem to use different polyadenylation sites. Sequence analysis of the cDNA clones corresponding to the 5.5-kb and 3.5-kb mRNAs indicates that the two bcl-2 transcripts carry two overlapping open reading frames, one of which is 717 nucleotides long and codes for a protein (bcl-2.alpha.) of 239 amino acids and a molecular mass of 26 kDa, while the other codes for a protein of 205 amino acids (bcl-2 $\beta$ , molecular mass 22 kDa) that is identical to bcl-2.alpha. except at the carboxyl terminus. The bcl-2 protein products in follicular lymphomas with or without bcl-2 rearrangements are identical to the normal bcl-2 products.

L22 ANSWER 36 OF 36 BIOSIS COPYRIGHT (c) 2008 The Thomson Corporation on  
STN

AN 1990:50171 BIOSIS  
DN PREV199089027535; BA89:27535  
TI STRESS-RESISTANCE CONFERRED BY HIGH LEVEL OF BCL-2-ALPHA PROTEIN IN HUMAN B LYMPHOBLASTOID CELL.  
AU TSUJIMOTO Y [Reprint author]  
CS THE WISTAR INST ANAT BIOL, 3601 SPRUCE ST, PHILADELPHIA, PA 19104, USA  
SO Oncogene, (1969) Vol. 4, No. 11, pp. 1331-1336.  
CODEN: ONCNES. ISSN: 0950-9232.  
DT Article  
FS BA  
LA ENGLISH  
ED Entered STN: 11 Jan 1990  
Last Updated on STN: 11 Jan 1990  
AB High levels of human bcl-2 protein(s) result in (i) the tumorigenic conversion of mouse NIH3T3 cells, (ii) the better survival of mouse

myeloid cells in the absence of the required growth factor and (iii) give a growth advantage to human EBV-lymphoblastoid B cells both in low serum medium and limiting dilutions. The effect of the high levels of bcl-2 protein in EBV-B cells was further investigated. This revealed that high levels of bcl-2 $\alpha$  protein made EBV-B cells more resistant to a variety of stresses including the application of heat shock, ethanol, methotrexate and the absence of serum. Stress resistance was not observed in EBV-B cells with elevated level of c-myc protein. The mechanism of stress resistance conferred by the bcl-2 $\alpha$  protein is yet to be determined although the resistance does not seem to be the result of an increase in major heat shock proteins, hsp70 and hsp90, nor the arrest of cells in G1/G0 phase. The increased viability was observed in control transfectants but not in bcl-2 transfectants when cells are seeded at higher density in the absence of serum. Thus the improved survival of cells as result of high levels of the bcl-2 $\alpha$  protein is not specific to the absence of growth factor but is found to occur with a variety of stresses.

=> s bcl 2 alpha (3a) mRNA  
L23 9 BCL 2 ALPHA (3A) MRNA

=> dup rem l23  
PROCESSING COMPLETED FOR L23  
L24 5 DUP REM L23 (4 DUPLICATES REMOVED)

=> d bib abs 1-  
YOU HAVE REQUESTED DATA FROM 5 ANSWERS - CONTINUE? Y/(N):y

L24 ANSWER 1 OF 5 CAPLUS COPYRIGHT 2008 ACS on STN DUPLICATE 1  
AN 1999:107273 CAPLUS  
DN 130:148830  
TI Growth hormone prevents human monocytic cells from Fas-mediated apoptosis by up-regulating Bcl-2 expression  
AU Haeffner, Astrid; Deas, Olivier; Mollereau, Bertrand; Estaquier, Jerome;  
Mignon, Alexandre; Haeffner-Cavaillon, Nicole; Charpentier, Bernard;

Senik, Anna; Hirsch, Francois  
 CS Equipe Immunologie Cellulaire Transplantation, CNRS-UPR 420,  
 Villejuif,  
 F-94801, Fr.  
 SO European Journal of Immunology (1999), 29(1), 334-344  
 CODEN: EJIMAF; ISSN: 0014-2980  
 PB Wiley-VCH Verlag GmbH  
 DT Journal  
 LA English  
 AB Apoptosis and particularly Fas-mediated apoptosis was proposed  
 to play a  
 key role in controlling monocyte homeostasis. The authors and  
 others have  
 documented the regulatory function of human growth hormone (hGH)  
 on  
 monocytic cells, which prompted us to investigate the role of  
 hGH on their  
 response to Fas antigen crosslinking. Using human promonocytic  
 U937 cells  
 constitutively producing hGH upon gene transfer and human primary  
 monocytes cultured in the presence of recombinant hGH, the  
 authors  
 demonstrated that hGH diminished Fas-mediated cell death by  
 enhancing the  
 expression of the antiapoptotic oncoprotein Bcl-2 as well as the  
 level of  
 bcl-2 $\alpha$  mRNA. In parallel, the  
 authors established that overexpression of Bcl-2 through gene  
 transfer  
 into normal U937 cells also diminished Fas-induced apoptosis.  
 As a result  
 of Bcl-2 overexpression, the authors found that hGH greatly  
 depressed  
 Fas-induced activation of the Cys protease caspase-3 (CPP32),  
 which in  
 turn affected the cleavage of poly(ADP-ribose) polymerase.  
 These data  
 provide evidence that hGH mediates its protective effect through  
 a  
 Bcl-2-dependent pathway, clearly a crucial step in enhanced  
 survival of  
 monocytic cells exposed to Fas-induced death.

RE.CNT 59 THERE ARE 59 CITED REFERENCES AVAILABLE FOR THIS RECORD  
 ALL CITATIONS AVAILABLE IN THE RE FORMAT

L24 ANSWER 2 OF 5 CAPLUS COPYRIGHT 2008 ACS on STN  
 AN 1999:360377 CAPLUS  
 DN 131:183383  
 TI Alzheimer's disease-related gene expression in the brain of  
 senescence  
 accelerated mouse  
 AU Wei, Xiaolong; Zhang, Yongxiang; Zhou, Jinhuan

CS Beijing Institute of Pharmacology and Toxicology, Beijing, Peop.  
Rep.

China

SO Neuroscience Letters (1999), 268(3), 139-142

CODEN: NELED5; ISSN: 0304-3940

PB Elsevier Science Ireland Ltd.

DT Journal

LA English

AB The levels of Alzheimer's disease (AD)-related genes, including  $\beta$ -amyloid precursor protein (APP), presenilin-1 (PS-1), PS-2,

apoE,

tau, c-fos, neural cell adhesion mol. 180 (NCAM-180), TGF- $\beta$ 1, IL-1 $\alpha$ / $\beta$ , IL-6, TNF- $\alpha$ / $\beta$ ,  $\alpha$ -2-Macroglobulin

( $\alpha$ 2M), class II major histocompatibility antigen Ia (MHCII Ia),

bcl-2 $\alpha$ , glucocorticoid receptor- $\alpha$  (GR $\alpha$ ) and

mineralocorticoid receptor (MR) mRNAs were determined by reverse transcription

polymerase chain reaction (RT-PCR) in the hippocampus and cerebral cortex

of senescence accelerated mouse (SAM). The levels of TGF- $\beta$ 1, IL-1 $\alpha$ , TNF- $\beta$ , c-fos, NCAM-180, PS-1 and APP mRNAs were normally expressed in SAMP8 compared with age-matched other subline that

is

resistant (SAMR1). The levels of apoE, GR $\alpha$  and MR mRNAs in the hippocampus of SAMP8, especially GR $\alpha$ , were evidently lower than

those in

the hippocampus of SAMR1. While bcl-2 $\alpha$ , PS-2 and tau mRNA

levels of

SAMP8 were significantly higher than those of SAMR1.

Inflammatory

cytokines (IL-1 $\beta$ , IL-6, TNF- $\alpha$ ),  $\alpha$ 2M and MHCII Ia antigen

mRNAs were not detected in the brain of SAM. The differences of

gene

expression in the cerebral cortex were less evident than in the hippocampus. The results indicated that some genes abnormally

expressed

in the AD brain were also found in the brain of SAMP8, which may contribute to its age-related deterioration of learning and

memory. The

authors' results also suggested that functional and pathol.

changes which

occurred in the brain of SAMP8 possessed some different aspects

in

comparison with the AD in consideration of the differences in

gene

expression.

RE.CNT 20 THERE ARE 20 CITED REFERENCES AVAILABLE FOR THIS RECORD  
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L24 ANSWER 3 OF 5 CAPLUS COPYRIGHT 2008 ACS on STN

AN 1996:647522 CAPLUS

DN 125:272311

OREF 125:50873a,50876a

TI Apoptosis and expression of bcl-2  $\alpha$  ,  
 $\beta$  mRNA isoforms and protein in neuroblastoma  
AU Mazzocco, K.; Scaruffi, P.; Gambini, C.; Negri, F.; Tonini, G. P.  
CS Advanced Biotechnology Center, G. Gaslini Institute, Genoa,  
16132, Italy  
SO Apoptosis (1996), 1(1), 63-68  
CODEN: APOPFN; ISSN: 1360-8185  
PB Rapid Science Publishers  
DT Journal  
LA English  
AB The authors studied apoptosis in 36 neuroblastomas by DNA ladder  
assay.

Expression of bcl-2 $\alpha$  and  $\beta$   
mRNA isoforms and protein were detected by RT-PCR and by  
immunohistochem., resp. Internucleosomal DNA fragmentation was  
found in  
20/36 (56%) tumor tissues collected both at onset and relapse of  
disease.  
Bcl-2 $\alpha$  and  $\beta$  mRNAs and protein were found in almost all  
examined  
tumors irresp. of DNA ladder, thus showing lack of correlation  
with the  
clin. stage. BCL-2 protein was observed to be expressed at  
various levels in  
undifferentiated and in more differentiated neuroblasts, while  
the stroma  
and the fibrovascular tissue were neg. The results show that  
apoptosis is  
present in neuroblastoma at all stages and that bcl-2 gene is  
widely  
expressed in tumor tissue. In this series of neuroblastomas,  
bcl-2  
expression was not correlated with unfavorable prognosis.

L24 ANSWER 4 OF 5 BIOSIS COPYRIGHT (c) 2008 The Thomson  
Corporation on STN  
DUPLICATE 2

AN 1994:127756 BIOSIS  
DN PREV199497140756  
TI Developmental regulation of bcl-2 expression in the thymus.  
AU Moore, N. C. [Reprint author]; Anderson, G.; Williams, G. T.;  
Owen, J. J.  
T.; Jenkinson, E. J.  
CS Centre Clinical Res. Immunology Signalling, Med. Sch., Univ.  
Birmingham,  
Birmingham B15 2TT, UK  
SO Immunology, (1994) Vol. 81, No. 1, pp. 115-119.  
CODEN: IMMUAM. ISSN: 0019-2805.  
DT Article  
LA English  
ED Entered STN: 24 Mar 1994

Last Updated on STN: 24 Mar 1994

AB An important factor in shaping the T-cell receptor (TcR) repertoire during thymocyte development is the susceptibility of double-positive (CD4+ CD8+) thymocytes to induction of apoptosis (negative selection) when the TcR is engaged by 'self'-antigens. Recent evidence has suggested that this susceptibility to apoptosis may be influenced by the expression of bcl-2, a proto-oncogene known to increase the resistance to apoptosis in various cell systems. Using a semi-quantitative polymerase chain reaction (PCR) technique in conjunction with staged embryonic material and purified thymocyte subpopulations we have investigated patterns of bcl-2 expression during normal T-cell development. Our results show that while bcl-2-alpha gene expression is readily detectable in immature CD3- CD4- CD8- thymocytes and in mature single-positive TcR-hi cells, it is drastically reduced in TcR negative double-positive (CD3- CD4+ CD8+) cortical thymocytes of intermediate maturity. Careful mapping of bcl-2-alpha re-expression in relation to the onset of TcR expression within the population of embryonic thymocytes indicates that bcl-2-alpha is up-regulated as soon as TcR molecules are expressed on the surface of CD4+ CD8+ thymocytes. Therefore, thymocytes susceptible to apoptosis on TcR ligation express bcl-2-alpha mRNA suggesting that changing levels of bcl-2 expression are unlikely to be the only determinant regulating susceptibility to apoptosis in the thymus. The possible implications of these changes in bcl-2 expression regarding other facets of thymocyte development will be discussed.

L24 ANSWER 5 OF 5 CAPLUS COPYRIGHT 2008 ACS on STN DUPLICATE 3

AN 1993:252039 CAPLUS

DN 118:252039

OREF 118:43710h,43711a

TI The bcl-2 gene is highly expressed during neurogenesis in the central nervous system

AU Abe-Dohmae, Sumiko; Harada, Nobuhiro; Yamada, Kazuyo; Tanaka, Ryo  
CS Med. Sch., Nagoya City Univ., Nagoya, 468, Japan

SO Biochemical and Biophysical Research Communications (1993),  
191(3), 915-21

CODEN: BBRCA9; ISSN: 0006-291X

DT Journal

LA English

AB An anal. method for quantitation of the RNA transcripts of  
murine bcl-2

gene was developed. The PCR products from bcl-2 $\alpha$  and bcl-2 $\beta$   
mRNA were fluorometrically analyzed and their specific contents  
were

calculated by the internal standard method. Both bcl-2 mRNAs in  
adult mice were

transcribed at the highest level in the thymus and at a  
comparable level

in the spleen. Aside from the immune system, the brain gave the  
most

abundant levels of the bcl-2 mRNAs. The ratios of bcl-2 $\beta$   
mRNA to bcl-2 $\alpha$  mRNA

in the thymus and spleen were significantly higher than those in  
other

tissues. During development of the brain, the bcl-2 $\alpha$  and  
bcl-2 $\beta$  mRNA levels were highest on embryonic day 15, and about

two  
and three times higher than those of adult, resp. The results  
suggest

that the bcl-2 gene functions to regulate development and  
survival of  
neurons in the central nervous system.

=> s 3 UTR and bcl 2

L25 69 3 UTR AND BCL 2

=> s 125 and PY<=1998

L26 8 L25 AND PY<=1998

=> dup rem 126

PROCESSING COMPLETED FOR L26

L27 4 DUP REM L26 (4 DUPLICATES REMOVED)

=> d bib abs 1-

YOU HAVE REQUESTED DATA FROM 4 ANSWERS - CONTINUE? Y/(N):y

L27 ANSWER 1 OF 4 CAPLUS COPYRIGHT 2008 ACS on STN

AN 1998:672675 CAPLUS

DN 129:271496

OREF 129:55245a,55248a

TI Viral vectors for identification of RNA regulatory sequences and  
interacting molecules

IN Blau, Helen M.; Spicher, Albert; Guicherit, Oivin

PA The Board of Trustees of the Leland Stanford Junior University,  
USA

SO PCT Int. Appl., 64 pp.

CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.
------------	------	------	-----------------

DATE

-----	----	-----	-----
-----			

PI	WO 9842854	A1	19981001	WO 1998-US6093
----	------------	----	----------	----------------

19980327 <--

W: CA, JP

RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC,  
NL, PT, SE

PRAI US 1997-42543P P 19970327

AB Methods and compns. for the identification, characterization and  
isolation

of regulatory RNA sequences are provided. Regulatory RNA  
sequences

mediate post-transcriptional regulation in response to various  
environmental conditions and can be used to alter the level of  
expression

of endogenous genes or to identify factors which interact with  
regulatory

RNA sequences. The invention addnl. provides improved vector  
systems for

rapid screening, anal., and tightly-regulated expression of  
regulatory RNA

sequences. The regulatory properties of highly conserved  
regions (HCRs)

within 3'-UTRs that have retained greater than 70% homol. within  
stretches

of 100 nucleotides over 30 million years were examined A  
retroviral vector

system was used with a selectable marker that allowed rapid  
delivery of

3'-UTR-reporter constructs to populations of thousands  
of cells within one to two weeks, avoiding problems associated  
with clonal

anal. and long-term selection. Addnl., this vector is modular,  
thereby

permitting direct comparison of different HCRs on gene  
expression,

independent of 5'-UTRs, promoters, protein coding regions and  
polyadenylation signals. Ten HCRs (from c-fos, c-myc,  
transferrin

receptor, bcl2, EF1 $\alpha$ , vimentin, ornithine decarboxylase,  
fibronectin, HuD and Ran genes) were examined Nine of these  
HCRs (i.e., all

except the Ran HCR) were found to decrease mRNA stability to  
different

extents. Two HCRs (the c-fos and vimentin HCRs) altered mRNA  
translation



under steady-state conditions. Four HCRs (the HuD, Ran, fibronectin and ornithine decarboxylase HCRs) mediated responses to changes in mitogen level by increasing reporter protein levels 2-fold while 2 HCRs exhibited a 6-fold difference in their response to another environmental stress, hypoxia.

RE.CNT 8        THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD  
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L27 ANSWER 2 OF 4 CAPLUS COPYRIGHT 2008 ACS on STN

AN 1997:607952 CAPLUS

DN 127:303779

OREF 127:59271a,59274a

TI Rapid molecular cloning of rearrangements of the IGHJ locus using long-distance inverse polymerase chain reaction

AU Willis, T. G.; Jadayel, D. M.; Coignet, L. J. A.; Abdul-Rauf, M.; Treleaven, J. G.; Catovsky, D.; Dyer, M. J. S.

CS Academic Department of Haematology and Cytogenetics, Haddow Laboratories,

Institute of Cancer Research-Royal Marsden Hospital, Surrey, SM2 5NG, UK

SO Blood (1997), 90(6), 2456-2464

CODEN: BLOOAW; ISSN: 0006-4971

PB Saunders

DT Journal

LA English

AB Clonal rearrangements of the Ig heavy chain (IGH) locus consisting of

either intrachromosomal VDJ rearrangements or interchromosomal translocations are a consistent feature of all B-cell malignancies and may

be used both diagnostically and to monitor response to therapy.

Many of

these rearrangements are targeted to the IGHJ segments, but only some can

be amplified with regular polymerase chain reaction (PCR)

techniques. To

permit PCR amplification of potentially all IGHJ rearrangements, we have

devised a method incorporating self-ligation of restriction endonuclease-digested DNA fragments with long-distance PCR

(long-distance,

inverse PCR [LDI-PCR]). We show here, using only 4 nested oligonucleotide

primers, the successful amplification and DNA sequencing of all IGHJ

rearrangements up to 5.4 kb in length from a panel of 13 cases and cell

lines of various types of B-cell malignancy. In all cases, both VDJ and

DJ IGH rearrangements and translocation breakpoints were amplified. Six cases exhibited t(14;18)(q32;q21). All translocation breakpoints were cloned and sequenced. Three cases exhibited a rearrangement to the BCL2 major breakpoint region (MBR). However, 2 other cases exhibited rearrangements between the MBR and the minor cluster region (mcr). These 2 cases broke within 44 bp of each other, confirming the presence of an addnl. 3' BCL2 breakpoint cluster region. The final case fell immediately 3' of the 3' UTR of the BCL2 gene adjacent to an Alu repeat. No other BCL2 breakpoints within this region have been reported. Four cases exhibited t(11;14)(q13;q32). All 3 cases with translocations targeted to the IGHJ segments were successfully amplified and sequenced, including 1 case in which the BCL1 translocation could not be detected by DNA blot using the currently available probes. All three translocation breakpoints fell outside the BCL1 major translocation cluster between 20 and 40 kb telomeric and showed no clustering. Two of the three fell within or adjacent to Alu repeat regions. LDI-PCR is a simple and robust technique that allows PCR amplification of nearly all IGHJ rearrangements.

RE.CNT 45      THERE ARE 45 CITED REFERENCES AVAILABLE FOR THIS RECORD  
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L27 ANSWER 3 OF 4 BIOSIS COPYRIGHT (c) 2008 The Thomson Corporation on STN

DUPLICATE 1

AN 1997:69518 BIOSIS

DN PREV199799368721

TI Cloning of the 3' end of rat bax-alpha and corresponding developmental

down-regulation in differentiating primary, cultured oligodendrocytes.

AU Madison, Dana L. [Reprint author]; Pfeiffer, Steven E.

CS Dep. Microbiol., MC-3205, University of Connecticut Sch. Med., Farmington,

CT 06030, USA

SO Neuroscience Letters, (1996) Vol. 220, No. 3, pp. 183-186.

CODEN: NELED5. ISSN: 0304-3940.

DT Article

LA English

OS Genbank-U59184  
ED Entered STN: 11 Feb 1997  
Last Updated on STN: 25 Mar 1997  
AB Bax-alpha is thought to form heterodimers with Bcl-2  
and prevent apoptotic cell death. A sequence was isolated from  
oligodendrocyte cDNA corresponding to the uncloned 3' end of the  
rat  
bax-alpha coding region and part of the 3' UTR via a  
degenerate polymerase chain reaction (PCR)-based cloning method.  
The rat  
bax-alpha clone is 96 and 91% homologous to mouse and human  
clones,  
respectively, and the 3' UTR demonstrates high  
homology with the cloned human 3' UTR. Northern  
analysis demonstrated that the 1.0 kb bax-alpha mRNA species was  
predominant. bax-alpha mRNA is expressed in mitotic,  
oligodendrocyte  
progenitors, and is subsequently down-regulated 2-fold in  
differentiating  
oligodendrocytes.

L27 ANSWER 4 OF 4 BIOSIS COPYRIGHT (c) 2008 The Thomson  
Corporation on STN  
DUPLICATE 2  
AN 1996:414837 BIOSIS  
DN PREV199699137193  
TI A bcl-2/IgH antisense transcript deregulates  
bcl-2 gene expression in human follicular lymphoma  
t(14;18) cell lines.  
AU Capaccioli, S.; Quattrone, A.; Schiavone, N.; Calastretti, A.;  
Copreni,  
E.; Bevilacqua, A.; Canti, G.; Gong, L.; Morelli, S.; Nicolin,  
A. [Reprint  
author]  
CS Dep. Pharmacol., Sch. Med., Via Vanvitelli 32, 20129 Milan, Italy  
SO Oncogene, (1996) Vol. 13, No. 1, pp. 105-115.  
CODEN: ONCNES. ISSN: 0950-9232.  
DT Article  
LA English  
ED Entered STN: 10 Sep 1996  
Last Updated on STN: 10 Sep 1996  
AB The 14;18 chromosome translocation, characteristic of most human  
follicular B-cell lymphomas, juxtaposes the bcl-2 gene  
with the IgH locus, creating a bcl-2/IgH hybrid gene.  
By mechanisms that are still under investigation, this event  
increases the  
cellular levels of the bcl-2 mRNA and thereby induces  
an overproduction of the antiapoptotic BCL-2 protein  
which is likely responsible for neoplastic transformation. In  
an effort  
to identify potential upregulators of bcl-2 activity  
in t(14;18) cells, we found, by strand-specific RT-PCR, a bcl-2  
antisense

transcript that is present in the t(14;18) DOHH2 and SU-DHL-4 but not in the t(14;18)-negative Raji and Jurkat lymphoid cell lines, and thus appears to be dependent on the bcl-2/IgH fusion. This antisense transcript is a hybrid bcl-2/IgH RNA, that originates in the IgH locus, encompasses the t(14;18) fusion site and spans at least the complete 3' UTR region of the bcl-2 mRNA. To achieve some insight into its biological function, we treated the t(14;18) DOHH2 cell line with oligonucleotides (ODNs) by specifically targeting the bcl-2/IgH antisense strand. These ODNs lowered bcl-2 gene expression, inhibited neoplastic cell growth by inducing apoptosis. We would like to propose the hypothesis that the bcl-2/IgH antisense transcript may contribute, by an unknown mechanism, to upregulation of bcl-2 gene expression in t(14;18) cells. The possibility has been considered that the hybrid antisense transcript mask AU-rich motifs present in the 3' UTR of the bcl-2 mRNA characterized in other genes as mRNA destabilizing elements.

=>

---Logging off of STN---

=>

Executing the logoff script...

=> LOG Y

COST IN U.S. DOLLARS	SINCE FILE	TOTAL
	ENTRY	SESSION
FULL ESTIMATED COST	224.86	350.03
DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE	TOTAL
	ENTRY	SESSION
CA SUBSCRIBER PRICE	-20.00	
-27.20		

STN INTERNATIONAL LOGOFF AT 16:28:40 ON 02 SEP 2008

Connecting via Winsock to STN

Welcome to STN International! Enter x:x

LOGINID:ssspta1633cxq

PASSWORD:

TERMINAL (ENTER 1, 2, 3, OR ?):2

\* \* \* \* \* Welcome to STN International \* \* \* \* \*  
\* \*

NEWS	1		Web Page for STN Seminar Schedule - N. America
NEWS	2	APR 04	STN AnaVist, Version 1, to be discontinued
NEWS	3	APR 15	WPIDS, WPINDEX, and WPIX enhanced with new predefined hit display formats
NEWS	4	APR 28	EMBASE Controlled Term thesaurus enhanced
NEWS	5	APR 28	IMSRESEARCH reloaded with enhancements
NEWS	6	MAY 30	INPAFAMDB now available on STN for patent family searching
NEWS	7	MAY 30	DGENE, PCTGEN, and USGENE enhanced with new homology sequence search option
NEWS	8	JUN 06	EPFULL enhanced with 260,000 English abstracts
NEWS	9	JUN 06	KOREAPAT updated with 41,000 documents
NEWS	10	JUN 13	USPATFULL and USPAT2 updated with 11-character patent numbers for U.S. applications
NEWS	11	JUN 19	CAS REGISTRY includes selected substances from web-based collections
NEWS	12	JUN 25	CA/CAPLUS and USPAT databases updated with IPC reclassification data
NEWS	13	JUN 30	AEROSPACE enhanced with more than 1 million U.S. patent records
NEWS	14	JUN 30	EMBASE, EMBAL, and LEMBASE updated with additional options to display authors and affiliated organizations
NEWS	15	JUN 30	STN on the Web enhanced with new STN AnaVist Assistant and BLAST plug-in
NEWS	16	JUN 30	STN AnaVist enhanced with database content from EPFULL
NEWS	17	JUL 28	CA/CAPLUS patent coverage enhanced
NEWS	18	JUL 28	EPFULL enhanced with additional legal status information from the epline Register
NEWS	19	JUL 28	IFICDB, IFIPAT, and IFIUDB reloaded with enhancements
NEWS	20	JUL 28	STN Viewer performance improved
NEWS	21	AUG 01	INPADOCDB and INPAFAMDB coverage enhanced
NEWS	22	AUG 13	CA/CAPLUS enhanced with printed Chemical Abstracts page images from 1967-1998